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# THE AMERICAN JOURNAL OF PHARMACY

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## EDITORIAL

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WELCOME, 1921.

Another annual cycle has been completed since, with the initial number of the Ninety-second Volume, we stood "On the Threshold of 1920" and extended to our readers and friends *Best Wishes and Heartly Greetings* and expressed the hope that the new year we were then entering upon would bring to them an abundant measure of Prosperity and Happiness. So thoroughly occupied have we been in the interim that we have scarcely noted even the succession of the seasons, but the rapid flight of time has brought us to another year of service and the initial number of another volume of the AMERICAN JOURNAL OF PHARMACY affords the opportunity of offering once more to our contributors and readers our Heartiest New Year Greeting.

The door has closed upon the events of 1920, yet, ere committing these to the realms of past history and to memory, we would fain take a parting view. We are cognizant of the fact that, while there have been many disturbing factors that caused the neglect of some of the Nation's opportunities, it has, nevertheless, been a year in which a goodly measure of substantial advancement has been made. The trend of the sciences and arts has been progressively upward and that of commerce and the industries has been toward a cessation of the speculative and the establishment of a sane basis of profit as a proper foundation for future advances. The drug trade has had its share of the prosperity as well as the perplexing trials of the period of readjustment and, on the whole, pharmacy has made wholesome strides in the right direction. We believe that the AMERICAN JOURNAL OF PHARMACY has contributed

its quota of service and we are thankful for the increased encouragement and support that has been accorded.

It is not our *forte* to peer into the crystal globe or to acquire a prophetic vision of what the year 1921 has in store. We acknowledge that we are imbued with optimism. A nation that is credited with 25 per cent. of the world's production has such a start on the highway of prosperity that, with but the exercise of customary energy and ingenuity coupled with the ethics of fair business, it should readily maintain its lead. We salute the new year. We welcome 1921 as another year of great opportunities with prospects of ample reward.

Let us impress upon our readers that to pharmacy will come its share of possibilities and the success and progress of our professional and trade interests during the year will be dependent entirely upon the energy and the concerted efforts of organized pharmacy. As we celebrate this year the centennial of the establishment of pharmaceutical education in America, it would appear that this was to be a year of golden opportunity for pharmacy. We earnestly appeal to every member of our calling to turn a new leaf; to this year honor pharmacy as never before and to be an honor to its ideals. We pledge anew the utmost efforts of the oldest pharmaceutical journal in America toward advancing the interests of pharmacy and making 1921 a year of phenomenal success.

With the commencement of this year we are pleased indeed to note the increased circle of contributors, patrons and readers, and to express our appreciation of the kindly interest manifested in our endeavors and our indebtedness to these for the broader field of usefulness thus placed at the command of the "Journal." We are happy to extend once more to all our sincere *Best Wishes* that 1921 will prove to be a year of unbounded Happiness and Prosperity.

G. M. B.

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## THE TREASURY DECISION ON TINCTURE OF GINGER.

Under date of November 16, 1920, the Commissioner of Internal Revenue issued the following declaration as Treasury Decision No. 3092.



*"To the Federal Prohibition Directors and Others Concerned:*

"On and after ninety days from the date hereof U. S. P. Tincture of Ginger, whether sold as Jamaica Ginger, Essence of Ginger, Extract of Ginger, or by whatever other name known, is hereby classed as a U. S. P. alcoholic preparation fit for use for beverage purposes, and may be manufactured, sold, transported and used only in the manner provided for other similarly classified official preparations listed in Section 60 (b) of Regulations No. 60 and Prohibition Mimeograph No. 87.

"Section 94 (a) of Article XVII of Regulations No. 60 is hereby revoked.

"An alcoholic extract of Tincture of Ginger made in accordance with the process described on Page 409, Ninth Revision of the U. S. P. will be classed as unfit for use for beverage purposes, provided the quantity of Ginger Root used is as follows:

"Jamaica Ginger No. 30 Powder, 400 grams to make 1000 millileters."

We are heartily in accord with the principle of prohibition that aims to prevent the use of alcoholic liquors as beverages and the misuse of medicinal preparations for such purpose. Nevertheless, we are compelled to question the wisdom of this departmental promulgation and likewise the authority for such an action.

Our contention has been always that the wording of Section 4 (b) of Title II of the Volstead Act was unfortunate, confusing and impracticable of enforcement, and until this error was corrected the medical and pharmaceutical professions, as well as the legitimate users of alcoholic liquid medicines will be subjected to continuous annoyance, hardships and the danger of prosecution. To legislate that medicinal preparations manufactured in accordance with formulas prescribed by the United States Pharmacopœia, National Formulary or the American Institute of Homœopathy must be "unfit for beverage purposes" is destructive to the art of pharmacy. Moreover, it is an inhumane indifference to the health of the people and savours of fanaticism instead of the prudent legislation expected of an American Congress.

*Fitness* is an attribute, a quality of a substance or preparation, that it is impractical to legislate against, but the improper use of such a substance or preparation is a proper and practical subject for legislative prohibition. No one doubts the "fitness" of water for drowning any human being, yet it would be the height of folly and ridiculous for Congress to enact that water must be rendered "unfit" for drowning before it could be consumed for the necessi-

ties of life. The intent of the legislation undoubtedly was to *prohibit the use of all alcoholic medicines for beverage purposes and all uncertainty could have been eliminated and the object attained if the advocates of prohibition had contented themselves with Congressional enactment of a prohibition of the purchase, sale, use, or possession of any alcoholic medicine, made by any formula, either in the authorities named or by any other recipe, for beverage purposes.*

*Fitness* is a question of individual opinion or taste that should not be incorporated in a law and much less handed over to a department for interpretation and enforcement. It is the sole duty of Congress to legislate on national questions and at times Congressmen and Senators have been greatly exercised over the encroachments of the executive departments upon the functions of the legislative bodies. Yet Congress has only too often itself stimulated departmental aggressions and bureaucratic government by engaging in the popular Washington game of "passing the buck" in leaving matters that should be determined in the enactment to rules and regulations to be framed by the enforcement division of one of the executive departments. Under these conditions the departments of the Government have assumed the authority to interpret the law and to frame rules and regulations that exceed oftentimes a fair construction of the enactment.

Congress cannot delegate its powers to legislate to any department and the granting of authority to frame appropriate rules and regulations for the proper enforcement of an act does not empower a department to make interpretations of the law. In a recent decision the Court again held "that the power given to a commissioner to frame rules and regulations gave no authority to make rulings interpreting the law and that any person relying upon any interpretation of the law made in a departmental ruling does so at his peril." In the same opinion it was again affirmed that "the meaning of the act is authoritatively determined by the Court and not by the Treasury Department."

The drug trade and the prohibition enforcement officers have joined in the endeavor by twistings, verbal gymnastics and subterfuges, and by interpretations of the language of this Section 4 not in harmony with the dictionary meaning of the words of the Act, to make the impracticable feasible. Would it not have been wiser

and more to the interest of all concerned if Congress had been frankly advised that this section of the Act was impracticable, inimical to health and public welfare and destructive of an essential industry in which alcohol was the most important raw material? The relief that is needed from the entangling and contradictory language can be afforded only by the law-making body and these forces should be united in urging upon Congress the necessity for a clarifying amendment that will permit the drug trade to carry on its legitimate manufacture and dispensing of medicines and the further development and progress of such an essential industry.

At the hearings held in Washington in December, 1919, it was at once apparent that the officials of the prohibition enforcement division assumed that, by virtue of the authority given in Section 1 (7) of the Volstead Act to the Commissioner of Internal Revenue to prescribe regulations for carrying out the provisions of this Act, they were empowered to determine what formulas of the United States Pharmacopœia, National Formulary or the American Institute of Homœopathy are fit for beverage purposes. The indictment of the eighteen official formulas subsequently listed in Regulations 60, Article XI, Sec. 60, was then foreshadowed. The medical and pharmaceutical professions were unexpectedly confronted by a new proposition by which the authority of these legally adopted works was to be questioned. Standard formulas constantly prescribed as remedial agents or as vehicles for medicines could, on the opinion of an official who might be but temporarily in office and without any special knowledge of the subject, be declared as fit for beverage purposes. *That the fitness of a preparation for perversion to improper use and not such improper use was to determine the possibility of its continued use as a medicine.* Some of the formulas so listed had never been viewed by the drug trade as possible tipples. The department realized that many of the formulas so listed were essential to the present methods of medical practice and so the officials assumed that they not only had the power to declare these as coming within the meaning of Section 4 as "not unfit for beverage purposes," but that they likewise had authority to declare that their manufacture could be undertaken

with non-beverage alcohol, but that the distribution and use of these must be under the same regulations as intoxicating liquors.

In T. D. 3092, the officials have gone one step further in assuming that they had the authority to modify a formula of the Pharmacopœia and to promulgate another formula as a standard. We believe that this a pure assumption and entirely without foundation of law. In the past, Congress has consistently denied to the enforcement officials the right to make standards and we fail to note anywhere in the Volstead Act that any such authority is vested in the Commissioner of Internal Revenue. Moreover, Congress, in the Federal Food and Drugs Act, made the standards and formulas of the U. S. Pharmacopœia and the National Formulary the legal standards for drugs and medicines and we do not concede that the Volstead Act or any other enactment has repealed this or placed it within the power of any department of the Government to either modify or nullify any of the provisions of that Act.

It becomes a matter of rather serious import when an official assumes that he can by edict undermine and destroy the authority of the Pharmacopœia and set aside any of its formulas. In this promulgation the Treasury Department is advising an infraction of the Federal Food and Drugs Act under which tincture of ginger entering interstate commerce must comply with the standard of strength and quality laid down in the United States Pharmacopœia and in following the provisions of this Treasury decision any person does so at his peril and doubtless could be prosecuted for violating the Act of June 30, 1906.

Since the pharmacopœial revision of 1880, tincture of ginger has been maintained at a 20 per cent. drug strength and evidently this, in the opinion of the medical and pharmaceutical specialists composing the committees of revision that successively passed upon this question, was the correct strength for a medicinal preparation. The Pharmacopœia is concerned solely with standards for medicines and its tincture of ginger is not intended as a culinary flavor or for any other purpose than medicinal.

If there are any reasons whatever why the formula for tincture of ginger should be changed after forty years' standing, such reasons should be presented to the committee of revision and the standard

changed by the proper procedure. As chairman of the sub-committee on tinctures the writer will welcome all suggestions for modifying the formula and will assure that these will receive careful consideration. He must, however, protest against any attempt at revision by departmental edict.

From the information at hand we are of the opinion that the officials of the Prohibition Enforcement Division were badly advised and the action of the Commissioner of Internal Revenue in the issuing of this decision was based upon insufficient evidence. The intent of this decision, to prevent the consumption of tincture of ginger as a beverage, is commended. If the tincture of ginger produced by any manufacturer was sold or consumed for intoxicating beverage purposes then it became the duty of said manufacturer to correct his methods of sale so as to prevent such illicit use, or accept the responsibility and become liable for the penalties provided in the law.

The proposition to denature this tincture by doubling the amount of drug contained may have been presented in a plausible manner, but we have no confidence in its effectiveness. It is doubtful if double the amount of ginger root can be extracted in accordance with the process described for the making of tincture of ginger in the U. S. P. Likewise, whether such a double strength preparation would be entirely suitable for medicinal purposes. Physicians at times have complained that the present official tincture of ginger is too strong. Moreover, by dilution with water and the use of a filtering medium, such double strength tincture can readily be made potable.

By revoking Section 94, paragraph (a) of Article XVII, Regulation No. 60, the restriction that Jamaica ginger may not be sold by retail druggists or other persons to the consumer in quantities exceeding one or two ounces at one time is rescinded and the unrestricted sale of the proposed double strength tincture of ginger will hereafter be permitted. There is every reason to believe that this will defeat the very purpose for which T. D. 3092 was promulgated. Already the druggists are being importuned by manufacturers to purchase ample supplies of this double strength tincture. With the unrestricted sale to be permitted this is prone to become

the most commonly used booze throughout the country, as by this decision it is classified as "unfit for use for beverage purposes" and may be sold promiscuously by any person.

The intent of the Volstead Act is to restrict the distribution of intoxicating liquors and alcoholic medicines to the licensed pharmacists and if this intent was carried out the distribution could be controlled and the illegal use of alcoholic liquors would be more promptly eliminated.

G. M. B.

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## ORIGINAL PAPERS

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### THYMOL AND CARVACROL PROBLEMS.\*

By D. C. L. SHERK.†

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#### EXTRACTION OF THE PHENOLS FROM ALKALINE SOLUTION.

In the separation of the phenols from the volatile oil of *Satureja hortensis*, L. Jahns<sup>1</sup> in 1882 first extracted the oil with 10 per cent. sodium hydroxide; recovered the phenols by acidification with hydrochloric acid, and again dissolved them in an equal volume of 15 per cent. sodium hydroxide. When this alkaline solution was extracted by shaking with ether repeatedly until nothing more came out, a phenol was removed which was proven to be carvacrol. This was *completely* removed from the alkaline solution by ether. Another phenol remained as completely in solution.

In 1899 Klages<sup>2</sup> made the observation, very interesting to him, that carvacrol as well as the isomer thymol can be removed from alkaline solution by steam distillation; and he also confirms Jahns' observation that the alkaline solution of the phenol could not be purified by extraction with ether; since the phenol is removed likewise. According to him, other phenols would not distill from alkaline solution.

\* From the laboratory of Edward Kremers.

† Fritzsche Bros. Fellow.

<sup>1</sup> Jahns, Ber. 15 (1882), p. 817.

<sup>2</sup> Klages, Ber. 32 (1899), p. 1517.

Raikow and Momtschillow<sup>3</sup> found that, among a considerable number of phenols, carvacrol and thymol are precipitated from alkaline solution by carbon dioxide. Of course, that would correspond to their inability to decompose carbonates to form phenol alkali derivatives. Following this up Raikow<sup>4</sup> studied a large number of phenols to determine their acidity and, among the various solutions employed as reagents, ammonia was found to dissolve carvacrol with no precipitation of a solid compound. Toward thymol it behaved in a similar manner. For this work, thymol was emulsified with warm water and this emulsion was employed in the tests. Water-glass was the only salt solution found that dissolved carvacrol, and in it the phenol is soluble to a considerable extent. There is no formation of a solid compound or precipitation of silicic acid. Thymol dissolves in water-glass also. Since these phenols are insoluble in carbonate solutions the solubility above cannot be attributed to alkali (carbonate), in the silicate. Perhaps this conclusion of Raikow should be modified, when it is considered that these solutions react distinctly alkaline and that hydroxide may actually exist in the solution. However, among the salt solutions one distinction between carvacrol and thymol was observed. Thymol is soluble in a solution of normal potassium phosphate,  $K_3PO_4$ ; while carvacrol is not.

Following Jahns' and Klages' observations, Stoermer and Kippe<sup>5</sup> found that the sodium compound of carvacrol may be extracted as such from 30-40 per cent. sodium hydroxide solution directly with ether. Thymol, and several other phenols mentioned, have the property of being extracted from alkaline solution with ether, petroleum, ether, ligroin, benzene, carbon disulphide and chloroform as the free phenol in only very small amounts.

In 1915 Boyd<sup>6</sup> determined the degree of hydrolysis of sodium phenoxides in aqueous solution in an attempt to determine their relative acidity. The method of Shields,<sup>7</sup> depending upon the rate of hydrolysis of methyl acetate, was adopted. In order that the

<sup>3</sup> Raikow and Momtschilow, *Chem. Ztg.*, 26 (1902), p. 1237; through *J. C. S.*, 841 (1903), p. 162.

<sup>4</sup> Raikow, *Chem. Ztg.*, 27 (1903), pp. 781, 1125.

<sup>5</sup> Stoermer and Kippe, *Ber.*, 36 (1903), p. 3992.

<sup>6</sup> Boyd, *J. C. S.*, 107 (1915), p. 1538.

<sup>7</sup> Shields, *Zeit. phys. Chem.*, 12 (1893), p. 167.

results might be compared with earlier work the hydrolysis was measured in  $N/32$  solution. The sparing solubility of some of the phenols made it necessary to employ solutions of much lower concentration and, since the hydrolysis constant was found to diminish somewhat with increasing dilution, a modified formula was used

$\frac{x^2}{(1-x)V^{7/8}} = \text{constant}$ , instead of  $\frac{x^2}{(1-x)V} = K_h$ , for calculating the observed results to a concentration of  $V_{32}$ .

#### RELATIVE ACIDITIES OF PHENOLS AT 25°.

	$K_h$ at $V_{32}$ .	Percentage hydrolysis at $V_{32}$ .	$K_a$ .
Phenol .....	0.000104	5.60	$1.15 \times 10^{10}$
Carvacrol .....	0.000267	8.83	$0.45 \times 10^{10}$
Thymol .....	0.000373	10.34	$0.32 \times 10^{10}$

$K_h$  is the hydrolysis constant for the sodium derivatives at 25° and  $V_{32}$  dilution. For carvacrol and thymol this was not obtained directly, but was calculated from the degree of hydrolysis by means of the formula

$$\frac{x^2}{(1-x)V} = K_h.$$

In column 2 are given the degrees of hydrolysis of the sodium derivatives of  $V_{32}$ , and the values for carvacrol and thymol were calculated from data obtained at higher dilution by means of the modified formula. Column 3 contains the dissociation constants  $K$ , for the free phenols in aqueous solution at 25°, calculated from the hydrolysis constants, according to the equation  $K = \frac{K_w}{K_h}$ ,  $K_w$ , the dissociation constant for water, being taken as  $1.2 \times 10^{-14}$ . The mean value for phenol calculated at the dilution at which it was determined becomes  $1.26 \times 10^{-10}$ , agreeing well with Walker's value of  $1.3 \times 10^{-10}$ .

In 1885 Lustig<sup>8</sup> prepared the sodium derivative of carvacrol by dissolving this phenol in 4 to 5 volumes of petroleum ether (b. p. 50-60°) and adding sodium. A lively evolution of hydrogen took place with a rise in temperature and a flocculent precipitate appeared. This dried to a fine white crystalline powder which decom-

<sup>8</sup> Lustig. Ber., 19 (1886), p. 11.



posed on addition of water or acids liberating carvacrol. On analysis by conversion into carbonate it gave the value for sodium of 13.64 per cent. The calculated value is 13.36.

In the laboratory the sodium derivative of both carvacrol and thymol were prepared in heptane and in ether. About ten grammes of the phenols were dissolved in 100 Cc. heptane and metallic sodium added. Carvacrol reacted with a slow evolution of hydrogen and a closely adherent coat formed on the metal. This liquid became reddish in color and a layer of the flaky precipitate adhering to the glass assumed an intense blue color. The bulk of the precipitate was of a pale color. Thymol caused an immediate more lively evolution of hydrogen and the temperature rose to 30-40°. The solution remained clear for a time and as soon as the first turbidity of crystals appeared the action began to slow down at once. This may be attributed to the fact that the phenols form complexes with the phenolates, the alkali derivatives.

Thus in 1903 Gentsch<sup>9</sup> obtained a patent on a process for obtaining double compounds of phenols with phenol alkali derivatives. These compounds result on treating the phenols, with or without an indifferent solvent, with alkali carbonates, caustic alkalis, or phenol alkali compounds, and were used for separation and isolation of phenols from mixtures. These crystalline derivatives may be washed and separated by progressive and differential solubility. Phenol forms a compound of the type  $C_6H_5OK \cdot 3C_6H_5OH$ , crystallizing from benzene or alcohol. Cresol also forms a complex. The existence of such a soluble complex may explain the effect of the addition of more thymol which dissolves the precipitate first formed.

The action of sodium on the phenols in ether was different from that in heptane. Ether which had stood over sodium was employed as a reaction medium using about the same quantities as for heptane. Sodium was added to the flask attached to a reflux condenser. Carvacrol developed the reddish color immediately and the action was so vigorous that the ether boiled. The sodium compound began to crystallize out as slender colorless prisms about a centimeter long. They were filtered off and placed in a lime desiccator where they became opaque and the edge became rounded, and the faces assumed a vitreous appearance. They quickly turned brown.

<sup>9</sup> Gentsch, D. R. P. No. 156 (1903), p. 761.

The ethereal solution was allowed to evaporate partially and the crystals filtered at the pump and dried as well as possible in a vacuum desiccator. The analysis indicates that excess carvacrol from the mother liquors remained on the crystals.

I.	0.7340	Gm.	gave	0.2303	Gm.	$\text{Na}_2\text{SO}_4$ .
II.	0.6685	Gm.	gave	0.2070	Gm.	$\text{Na}_2\text{SO}_4$ .
Sodium calc. for $\text{C}_{10}\text{H}_{11}\text{ONa}$ .						Found.
Per cent.						Per cent.
13.36						I. 10.16
						II. 10.03

The crystals were dissolved in ether and this solution diluted with benzene and the ether allowed to evaporate. The sodium compounds slowly turns greenish in the air. It dissolves in ether with absorption of heat. With loss of ether fine, colorless prisms appeared and were filtered at the pump; washed with benzene to remove excess of carvacrol and dried in a vacuum.

The melting point of these crystals was 72-73° and decomposition took place very readily. For analysis it was dried at 50° for five hours when a brownish color had begun to develop.

I. 0.5668 Gm. lost 0.060 Gm. and gave 0.2016 Gm.  $\text{Na}_2\text{SO}_4$ .  
 II. 0.7395 Gm. lost 0.0814 Gm. and gave 0.2635 Gm.  $\text{Na}_2\text{SO}_4$ .  
 III. 0.6549 Gm. lost 0.0626 Gm.  
 Loss on drying: I. 9.57 p. c.  
 II. 9.92 p. c.  
 III. 9.56 p. c.  
 Sodium I. 11.51 p. c. on dried basis 12.75 p. c. calc. 13.36 p. c.  
 II. 11.54 p. c. on dried basis 12.79 p. c.

These results correspond to the formula  $C_{10}H_{13}ONa$  as the composition of the compound obtained from ether.

Thymol reacts with sodium in ether in a lively manner but nothing could be crystallized out. Metallic sodium remained bright in the solution which was clear and almost colorless. It began to oxidize on long standing.

Carvacrol is completely extracted from alkaline solution by repeatedly shaking with ether. The ether was evaporated on the waterbath and in this way water was retained by the carvacrol. This material was obtained by working up a Monarda oil with 5 per cent. sodium hydroxide. To ascertain the amount of sodium in the carvacrol, presumably extracted as carvacrolate, a quantity of the clear phenol was evaporated and the residue ignited in a

crucible at a just perceptible red heat. The carvacrol carried only about 0.01 per cent. of non-volatile material.

I. 8.775 Gms. carvacrol gave 0.0007 Gm. non-volatile residue.	
II. 8.675 Gms. carvacrol gave 0.0010 Gm. non-volatile residue.	
Non-volatile residue.	Percentage.
I .....	0.009
II .....	0.012

It thus becomes apparent that from a solution of carvacrol in five per cent. sodium hydroxide the free phenol alone is extracted by ether.

In continuation of this work the behavior of various other solvents toward thymol in alkaline solution was determined on a somewhat more exact basis under conditions which would resemble those actually employed in the extraction of thymol from oils used as a source of the phenol. The use of 5 per cent. sodium hydroxide has been recommended for the assay of phenol-containing oils and also for extraction in preparation of the phenols and for analytical separations.

An alkaline solution was prepared from sodium hydroxide made by hydrating the metal to keep the product free from carbonate. Sodium was placed in a nickel dish covered with a layer of paraffin oil about 5 cm. deep in a casserole and a funnel just fitting into the casserole but over the dish covered the whole. A dropping funnel allowed water to run slowly on the metal. This solution was made up to 5 per cent. strength and standardized. When, however, the alkaline solution of thymol was prepared by adding one equivalent of the phenol, expansion took place almost equivalent to 1 Cc. per Cm. of thymol.

Vol. of alkali solution .....	840 Cc.	.....
Equivalent of thymol .....	.....	157 Gms.
Vol. of solution after .....	985 Cc.	.....
Increase .....	.....	145 Cc.

All of the thymol did not go into solution, however, and after continued shaking it was filtered and the residue recovered. The hydrolysis of the thymol sodium compound at these dilutions would effect also the amount taken into solution, as thymol itself is extremely slightly soluble in water. In view of this fact and because of the ease with which it is removed by ether a quantitative estima-

tion of thymol was made by weighing the thymol recovered after acidification and extraction with ether and evaporation of the solvent. In the further operations of extraction the thymol recovered was weighed after the solvent had been distilled off and thymol crystallized and allowed to stand in a vacuum desiccator until the weight became constant.

The accuracy of this method was investigated. One gramme of thymol was dissolved in 50 Cc. of anhydrous ether and distilled from a weighing flask in a hot water bath as long as ether came over. Then it was transferred to a vacuum desiccator over calcium chloride. The difference in weight was attributed to volatility of thymol with the vapor of the solvent under the conditions of the experiment.

A series of weighings on two samples carried out over sixteen days showed the following losses toward the end of the experiment:

Sample 1,000 g.				
	I.	Loss per	II.	Loss per
	Gms.	day.	Gms.	day.
		Gms.		Gms.
Weighed .....	30.6863	.....	27.5524	.....
Feb. 4 .....	30.83+	.....	27.68	.....
Feb. 6 .....	30.7066	.....	27.5652	.....
Feb. 14 .....	30.6946	.....	27.5524	.....
Feb. 18 .....	30.6692	0.0062	27.5266	0.0064
Feb. 19 .....	30.6660	0.0032	27.5256	0.0010
Feb. 20 .....	30.6676	gain	27.5253	0.0003
Total recovery ....	97.97 p. c.		97.33 p. c.	

The ether distillate was tested for thymol by Flueckiger's test and 10 Cc. gave a positive reaction but the chloroform layer retained no pink or violet color indicating only slight quantities of thymol.

In this series it was noticed that the thymol remained fluid during the entire 16 days and only solidified after inoculation. Another series was run starting with moist ether that was standing over a layer of water in order to duplicate more closely the conditions of extraction of solutions where the ether is recovered in the moist condition. One gramme of thymol was dissolved in 50 Cc. and the ether distilled off and weighings made. After standing over night in the open air, the residue was seeded and weighings continued.

Sample 1,000 g.				
	I.	Loss per	II.	Loss per
	Gms.	day.	Gms.	day.
		Gms.		Gms.
Weighed .....	30.6863	.....	27.5523	.....
Feb. 21 .....	30.6844	.....	27.5506	.....
Feb. 22 .....	30.6820	0.0024	27.5488	0.0018
Feb. 24 .....	30.6750	0.0035	27.5423	0.0032
Recovery .....	99.57 p. c.		99.65 p. c.	

When the loss decreased per day to about 0.002 Gm. weighings were discontinued as the loss then became regular indicating sublimation of thymol as the single factor.

When the thymol recovered with dry ether is inoculated or otherwise induced to crystallize the normal rate of loss is established very much more quickly and recoveries of 99.09 and 98.47 per cent. were obtained.

This tendency of thymol to remain fluid was not alone characteristic of the solvent, ether, because as soon as the beneficial effects of crystallization were established all samples were inoculated. The heat of fusion was also efficient in removing the last traces of solvent and unless solidifying spontaneously, thymol was only inoculated after two days.

One characteristic of thymol is, however, its avidity for ether because fresh crystals of thymol exposed along with the evaporated ether solution in the desiccator took up enough ether to liquefy themselves. The other solvents were exposed in a similar manner but none caused this "deliquescence" of thymol. There is every reason to assume also that this supercooled thymol has a higher vapor tension and a corresponding higher rate of loss than the solid.

For extraction of the alkaline solution 50 Cc. were shaken with 50 Cc. solvent and this repeated twice with fresh portions of solvent. The cylinder containing the two was shaken vigorously for one minute and allowed to stand for three minutes to clear and shaken again one minute allowing two minutes for clearing and finally shaken again for one minute. These conditions were observed throughout the work.

The solution was emulsified as well as possible and transferred to a separatory funnel and the solution run off; the solvent poured off, and the funnel washed down with the solution, and allowed to drain. About two Cc.'s of solvent were used to wash the funnel

and added to the solvent. There was a slight loss of solution in these manipulations but the diminution in volume with loss of thymol from the solution and the amount taken up by the solvent always exceeded this quantity.

		Ether.		Heptane.	
		A.	B.	A.	B.
		Cc.	Cc.	Cc.	Cc.
1st Extn.	Vol. of aqueous soln . . . . .	50.0	50.0	50.0	50.0
	Vol. of aqueous layer . . . . .	44.7	45.0	49.3	49.1
2d Extn.	Vol. of aqueous soln . . . . .	44.0	44.7	49.0	48.9
	Vol. of aqueous layer . . . . .	42.7	43.0	48.5	48.4
3d Extn.	Vol. of aqueous soln . . . . .	42.0	42.6	48.3	48.4
	Vol. of aqueous layer . . . . .	41.2	41.5	47.7	47.6

The various solvents employed were purified in approved manners. The ether was washed with dilute alkali; dried over calcium chloride and, after standing over sodium, distilled in a dry apparatus. The heptane was a very pure sample previously purified by hydrogen-bromide and had stood over sodium several months. It was used without distillation and probably boiled originally within one degree. The benzene was dried over sodium and distilled. The carbon tetrachloride and disulphide both were washed with dilute alkali and dried by standing over calcium chloride about a week. These commercial products were finally distilled to complete purification.

The amount of thymol as determined by acidification and extraction with ether and weighing after recovery of ether was 7.459 Gms. in 50 Cc. of solution. The concentration of alkali was 4.188 per cent. According to Seidell<sup>10</sup> thymol is soluble in water at 22° to the extent of 0.0936 Gm. per 100 Cc. and at 25° of 0.0981 Gm.; while in dilute hydrochloric acid such as resulted above the solubility is less. Extraction with ether would remove that also. As a rough check on the results of extraction except in the case of ether, the remaining alkaline solution was acidified and the thymol weighed after drying in the air over night, or until it became fairly constant.

<sup>10</sup> Seidell, A. C. J., 48 (1912), p. 453.

Solvent.	1st Extraction		2nd Extraction.		3rd Extraction		Total Extraction Per cent.	Decrease in Volume.			Percentage of total re- maining in solution extracted each time.			
	Wt.	Per cent.	Wt.	Per cent.	Wt.	Per cent.		1st. Cc.	2nd. Cc.	3rd. Cc.	1st.	2nd.	3rd.	
Ether	A	6.043	81.02	1.170	15.68	0.219	2.93	99.89	5.3	1.3	0.8	81.0	82.6	88.9
	B	6.031	80.86	1.106	16.03	0.223	2.98	99.63	5.0	1.7	1.1	80.9	83.8	95.9
	A	6.003	81.79	1.008	14.72	0.167	2.28	98.66	5.6	1.6	1.0	81.8	80.8	66.7
	B	6.172	82.75	1.136	15.23	0.184	2.47	100.45	5.4	1.4	1.2	82.3	90.3	122.4
Heptane	A	1.103	14.80	0.603	8.09	0.521	6.99	29.86	0.7	0.5	0.6	14.8	9.5	9.1
	B	1.041	13.95	0.673	9.03	0.522	7.00	29.98	0.9	0.5	0.8	14.0	10.5	9.1
Benzene	A	2.736	36.68	1.346	18.04	1.007	13.49	68.21	3.0	1.4	1.2	36.7	28.5	29.8
	B	2.700	36.20	1.336	17.91	1.001	13.41	67.53	2.8	1.8	1.3	36.2	28.1	29.2
Carbon Tetra-Chlor-														
ide	A	2.285	30.57	0.962	12.90	0.687	9.21	52.74	2.3	0.9	0.9	30.6	18.6	16.3
B		2.263	30.34	0.970	13.00	0.683	9.16	52.50	1.8	1.2	0.4	30.3	18.7	16.2
Carbon Disulphide	A	2.559	34.18	1.493	20.02	0.956	12.81	67.02	2.6	1.1	0.1	34.2	30.4	28.0
	B	2.548	34.17	1.468	18.87	0.922	12.36	65.39	2.2	0.2	0.3	34.2	28.7	26.3

The results with ether bear out the conclusions of previous workers. Thymol is completely and somewhat readily removed from a dilute alkali solution with ether and after three extractions with about equal volumes of ether, practically no thymol remains in solution. Apparently in every case it was recovered as the free phenol and readily obtained crystalline. Heptane is the most indifferent solvent chemically and extracts the least amount of thymol. This is in accord with the observations previously made that it exhibits a striking selective solvent action in many cases. It would be very valuable in purifying an alkaline solution obtained in extracting thymol from an oil. Thymol recovered by the use of carbon disulphide seemed to be the brightest and of the most pleasing appearance. There is some color developed in the alkali and carbon disulphide reacts with the dilute alkali because hydrogen sulphide is given off on acidification for recovery of thymol. However, benzene is about equally effective as a solvent.

The increasing concentration of alkali with diminution of thymol content does not seem to effect ether, and benzene and carbon disulphide respond slowly, but heptane and carbon tetrachloride are effected very considerably. This fact is also of interest in the assay of phenol-containing oils by means of dilute alkali where heptane is used to prevent the formation of emulsions and permit easier and quicker readings of the volume remaining unabsorbed.

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## SPIDERS USED IN MEDICINE.

By J. T. LLOYD, PH.D.

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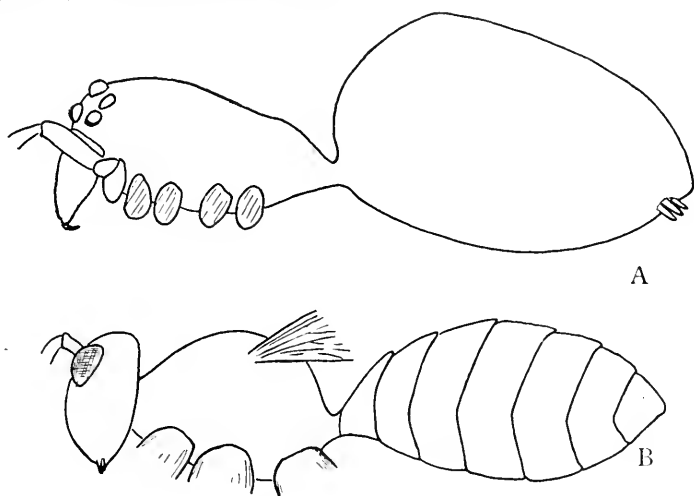
That insects and their by-products, such as shellac and honey, play an important part in the economy of man, is known to all. Perhaps, however, it is better known to the physician than to the layman, that a few spiders play their role in the practice of medicine. These spider remedies, like the insect medicines, are not of modern origin. In old works one finds frequent references to cobweb, which was then administered in the form of pills instead of the modern alcoholic pharmaceutical preparation, *Tela Araneæ*.

In the popular mind there is often little knowledge of the distinctions between spiders and insects, although the class *Arachnida*



(to which the spiders, but not the insects, belong) contains several orders, such as the scorpions, that are closer akin to the spiders than are the insects. Most of these are so distinct in superficial appearance that there is little probability of their being mistaken for spiders.

If one will remember that spiders have four pairs of legs, apparently no antennæ, and that their head is not separated from the thorax by a neck-like constriction, there need be no trouble to distinguish them from insects; which have three pairs of articulated legs, one pair of antennæ, and head and thorax separated by a distinct "neck." In the class Arachnida, spiders may be easily separated from other orders by remembering that thorax and abdomen are separated by a short, slender stalk, and the abdomen is not segmented. In their nearest relatives, the mites, the thorax and abdomen are fused and sack-like.



(A) **Diagram of a Spider.** The head and thorax are fused, the abdomen is not segmented; there are four pairs of legs; there are no antennæ, but a pair of leg-like pedipalps arises in front of the first pair of true legs.

(B) **Diagram of an Insect.** The head and thorax are separated by a "neck"; the abdomen is segmented; there are but three pairs of legs; a pair of true antennæ arises from the head in the region of the eyes.

Since very early times many people have looked upon spiders with unfounded dread and superstition. During the medieval

period, "Tarantism," a contagious disease that was common in southern Europe, especially Italy, was believed to have been started by the bite of a spider. The victims of this disease were possessed with an uncontrollable desire to dance. In our own day and among our own people it is not unusual to blame the bite of a spider for swellings or itchings of unknown origin, but when questioned the sufferer is invariably unable to give other evidence that a spider is responsible for the trouble, than the usual answer, "What else could have done it?" On this negative evidence the blame is fixed for about one hundred per cent. of the "spider bites" of our people.

With the possible exception of a single species\* in our Southern States, and the true tarantulas of the Southwest, it seems safe to accept that there are no spiders in our country whose bite need be in any way feared. The writer has handled large numbers of our native spiders, as well as (during excursions in the tropics) hundreds of the "banana tarantulas," which are not true tarantulas, but harmless spiders of a different family. True tarantulas may sometimes, however, be found in banana bunches. In no case has the writer been bitten, and frequent attempts to induce spiders to bite the tender skin between his fingers resulted in failure. Others who have made this experiment with success report that the wound inflicted is no more painful than a slight prick with a needle. That spiders do inject a virus into their victims is indisputable, but it is in quantities sufficient only to paralyze an insect. Besides, it is injected so slowly that little, if any, could be secreted during the short interval that the "jaws" remain in the wound of an animal as large as man.

*Spider Web.*—All species of spiders are capable of spinning web, though far from all spin orbs or sheet-like webs for entrapping prey. Many species only throw out a "drag line" as they move from place to place, or drop from surface to surface, and never spin a more complex web, except in wrapping their egg masses.

The web material, or silk, is produced in large glands within the spider's abdominal cavity. In the glands the material is liquid or mucilaginous, but (except certain parts of the viscid silk) immediately hardens on exposure to the air. From the glands it passes

\* *Latrodectus mactans*, a jet-black spider with markings of yellow or red.

to the exterior through silk ducts, which often open on movable, finger-shaped "spinneretts."

In all, spiders produce seven distinct kinds of silk; some thread-like, some band-like, some viscid, some dry. Though most spiders secrete more than one kind of silk, and some spiders secrete several kinds, no one spider secretes all seven. Each kind of silk originates in its own distinct glands and passes to the exterior through its own opening.\*

For pharmaceutical preparations an attempt is made to collect the sheet-like webs of *Coras medicinalis* (*Tegenaria medicinalis*) from the corners of rooms in warehouses and kindred places. It is probable, however, that the webs of the several species of dwelling-inhabiting spiders enter into all pharmaceutical preparations of web. No collector of webs could be expected to possess technical knowledge sufficient to enable him to distinguish species. If he should possess the required knowledge, it would be impracticable for him to take the time to apply his training for the examination of each web collected. Nor is there need for such discrimination. No reason why the web of one species of dwelling-inhabiting spider should be of different therapeutical qualities from another, has ever been recorded.

We do not know that a chemical analysis of spider web has ever been made. Tests given pharmaceutical preparations, however, show an absence of sugar, but give a slight reaction to Mayer's test for alkaloid. This is true also of tincture we have prepared from fresh web. The therapeutic value of the preparation may be in part due to this alkaloid.

In the present-day practice of medicine the large spiders of the sub-family *Aviculariinae*, commonly known as "tarantulas," or "bird spiders," are employed by Homœopathic physicians. Under the name of *Mygale lasidora* the Pharmacopœia of the American Institute of Homœopathy, 1897, page 408, gives directions for preparing the tincture of the "whole spider." Other references to the preparation and use of *Mygale* (tarantula) are given in Allen's "Encyclopedia of Pure Materia Medica," Vol. VI, 1877, and elsewhere.

\* A careful and interesting account, written in non-technical language, of the habits, anatomy and classification of spiders, may be found in *The Spider Book*, by John Henry Comstock, Doubleday, Page & Co., 1912.

*Spider and Spider Web in Medicine.*—At least since the time of Pliny (first century A. D.) literature on medicine abounds in references to the use of spiders and their webs. The ideas of most of the old authors concerning the medicinal use of spiders, as may be noted in the following quotations, seem little more than “charm medicine” or superstition. Let us quote:

*Spiders.* “The fly-catching spider, wrapt in a linen cloth and hanged on the left arm, is good to drive away a Quotidian, saith *Trallianus* (sixth century, A. D.). But better if any of them be boiled with oil of bay to the consistence of a liniment; if you anoint the arteries of the wrists, the arms and temples before the fit, the fever abates and seldom comes again. *Koronides* or *Koranus*.\* A spider bruised with a plaister and spread on a cloth and applied to the temples, cures a tertian. *Dioscorides* (first or second century, A. D.). The spider called *Lycos*, put in a quill, and hanged on the breast doth the same. *Pliny* (first century, A. D.). That house spider that spins a thick fine and white web, shut up in a piece of leather or a nut-shell, and hanged to the arm or neck, is thought to drive away the fits of a quartane. *Dioscorides* saith he proved it to be true. Three living spiders put into oil, let them presently boil on the fire, drop some of that oil warm into the ear that is in pain, and it profits much. Or press out the juice of spiders with juice of roses, and put it in with wool. *Marcellus Empiricus* (380-408, A. D., or later). Pliny bids infuse them in vinegar or oil of roses and stamp them and then drop some into the ear with saffron, and it will still the pain certainly: *Discorides* affirms as much. *Sofratus* . . . saith, that *Cranacolapsus* (a certain spider) drowned in oil, is a present remedy against poisons, as the Scholiast of *Nicander* (second century, B. C.) professeth. *Aetius* (about 500, A. D.) for suffocation of the mothers, applied a cerate of spider to the navel, and said it did great good.”

*Spider Web.* “The spider’s web is put into the unguent against Tetters, and applied to the swellings of the fundament, it consumes them without pain. *Marcellus Empiricus*. Pliny saith it cures runnings of the eyes, and laid on with oil, it heals up wounds in the joints. Some rather use the ashes of the webs with Polenia and wine. Our chirurgians (surgeons) cure warts thus: They wrap a spider’s ordinary web into the fashion of a ball, and laying it on the wart, they set it on fire, and so let it burn to ashes, by this means the wart is rooted out by the roots, and will never grow again. *Marcellus Empiricus* was wont to use the web of spiders found in the Cypress tree in a remedy for the Gout to ease the pains.”—*Mouffet*, “*The Theater of Insects*,” 1858, page 1023.

A few of the early writers, like Antoninus Pius, and more during the medieval period, used the web to stop the flow of blood.

\* King of Persia, who wrote a work on natural history.

For this purpose it was also used by the American Indians, as well as in domestic practice, no doubt with a real value. For example:

"Antoninus Pius (86-161, A. D.) was wont to say, that the quirks of sophistry were like to Spiders' Webs, that had a great deal of art and ingenuity in them, but very little profit. But how often hath the blood run forth from the body most miserably by a fresh wound? Yet it had been easy to have stopped it by laying on a spider's web."—Mouffet, *"The Theater of Insects,"*

"*Telia Arancarum, Cobweb.*—Every one knows what this is, and how produced. It appears not in medicinal prescriptions, but as accident, for want of other helps, has taught its use to common people for stopping blood in a fresh wound. And this it seems to do by its extraordinary fineness; which makes it adhere to, and top up the mouths of the vessels, so as to prevent the effusion of their costents."—*Quincy's Compleat English Dispensatory*, 1749.

"*Arancarum Telæ Pharm. Edinb., Cobwebs.* These are applied by the common people for stopping the bleeding of wounds; which the effect, not by any styptic power, but by adhering to the part, and closing the orifices of the vessels."—*Levis' Materia Medica*, London, 1768.

"The web astringes and conglutinates, and is, therefore, vulnerary; restrains bleedings, and prevents inflammation. The country people have a tradition, that a small quantity of spider's web, given about an hour before the fit of an ague, and repeated immediately before it, is effectual in curing troublesome, and sometimes obstinate distemper. This remedy is not confined to our own country, for I am well informed that the *Indians* about *North Carolina* have great dependence on this remedy for agues, to which they are much subject; and I am acquainted with a gentleman long resident in those parts, who assures me he was himself cured by it of that distemper. And, indeed, experience confirms the efficacy of this medicine in the cure of agues."—*James, New English Dispensatory*, London, 1747.

In May, 1809, The Medical and Physical Journal of London published a long article by Dr. Robert Jackson, calling to the attention of the profession the medicinal use of spider web, or cobweb, in the treatment of intermitting fevers. Frequent references have been made to this article by subsequent publications in Europe and in America. After Dr. Jackson's publication, the use of spider web in the treatment of malarial fevers seems to have been neglected until about 1865, when articles by Dr. L. M. Jones appeared in "The Lancet and Observer," Cincinnati, and in Jones and Scudder's *Materia Medica*. These again brought it to the attention of physicians:



grav. (1.146); acid number 48.8; saponification number 356, cinnamein content 70 per cent. and saponification number for the separated cinnamein 382. The saponification number of the balsam as well as the saponification number of the cinnamein are too high. For normal balsams they are not higher than 260. The acid number is too low. Hence an adulteration with an ester was probable. On account of the high saponification numbers, adulteration with the methyl ester of benzoic acid or with an ester of a di-basic acid was expected. In order to determine this matter to a certainty the aromatic ester was separated from a larger sample of the balsam.

By saponifying a part of this ester with alcoholic potash ( $\frac{1}{2}$  normal) needles were obtained, which were collected and dissolved easily in water. The solution was acidified and separated on standing a crystalline powder, which when heated with resorcinol and sulphuric acid could be converted into fluorescein. The powder was therefore phthalic acid. Fractional distillation showed that the aromatic esters distilled for the larger part at  $282^{\circ}$ - $286^{\circ}$ . It is therefore probable that most of it consisted of the dimethylester of phthalic acid, which has often been reported as an adulterant for cinnamein and essential oils. The adulteration is so obvious, that quantitative tests are not even necessary for its identification.

If one drop of the balsam is heated to boiling with 100 milligrams resorcinol and 10 drops of sulphuric acid, fluorescein is formed which is easily detected on addition of alkali. As charring occurs it is recommended to dilute the heated liquid with water before adding the sodium hydroxide solution. The fluorescence is obtained in this way between the layers.

Pure balsam treated in this way only shows a weak fluorescein reaction.

The adulterated balsam, which as I afterwards was informed is put on the market as *Balsamum peruvianum syntheticum*, may also be recognized by the test published by Dietrich (*Ber. d. Deutsch. pharm. Gesell.* 1908, p. 142), as follows: 500 mgm. to 1 gm. balsam are dissolved in ether and shaken with 2 per cent. NaOH. By adding acid to the alkaline solution the resins are separated. These resins are dissolved in ether and carefully poured on sulphuric acid. Genuine peru balsams will never show a green or blue layer, not even

after adding hydrochloric acid to the ether-sulphuric acid layers. The adulterated balsam showed a blue colored layer.

One of our pharmaceutical firms supplied me with benzoyl-benzoate, which according to the statement of the firm, was used for the preparation of substitutes for peru balsam. It is obvious that if benzoyl-benzoate is used for adulteration a normal number for the saponification number of the cinnamein is found on analysis as benzoyl-benzoate is one of the principle constituents of cinnamein. However, I found that the received benzoyl-benzoate and also a preparation of one of the laboratories of our university showed a strong fluorescein reaction with resorcinol and sulphuric acid, probably because the preparations were made with benzoic acid, prepared from phthalic acid. Anyhow, an adulteration may be detected by this test.

Another product, appearing on the market as *Balsamum peruvianum syntheticum* (the manufacturers seem to have a peculiar notion of the word synthesis) gave on analysis by my assistant Miss M. le Coultre, the following results:

Acid number .....	48.1
Saponification number .....	220.4
Cinnamein in % .....	64.0%
Saponification number of the cinnamein .....	254
Refractive index of the cinnamein .....	1.5682

From a mixture of 3 vol. of this balsam and 1 vol. carbon-disulphide a kind of jelly separated out.

Five drops of balsam shaken with 8 cc. petroleum ether separated a powder, and some of the balsam stuck to the walls of the tube.

The fluorescein reaction was stronger than with the unadulterated balsam. Dietrich's test gave a pretty green ring reaction which became greenish blue on addition of hydrochloric acid.

Notwithstanding the normal figures obtained with the quantitative analysis, this preparation was recognized by the qualitative tests as an artificial product. It was made undoubtedly with benzoyl-benzoate.

I was told that genuine peru balsam did not find buyers; whereas, the so-called synthetic preparations were easily sold. I hope that the Dutch apothecaries will keep their high standing by not buying these preparations.



## AN EPOCH MAKING DISCOVERY.

BY CHARLES H. LAWALL, PH.M.,

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It is bromidic to quote the oft repeated proverb about the prophet and his own country, and yet none other is applicable to the situation in which Einstein finds himself in Germany while much of the remaining scientific world is doing him homage and discussing his work on "The Special and General Theory of Relativity."

This is an age of pragmatism and while the educational attainments of the average individual are higher than ever before in the world's history, it is to be doubted whether there is much sympathy with, or consideration of, abstract principles as a rule, except among mathematicians and physicists.

From the earliest times there have been those who went out of their way to grapple with the unknown, whether or not the rewards were apparent. Babylonian arithmeticians and Egyptian geometers had exercised their mathematical abilities chiefly along the lines of mensuration, with some attention to astronomy, but when the speculators of Hellenic Origin appeared, abstract mathematics became a cult which lasted for several centuries and which influenced human thought for all time. Thales, Pythagoras, Plato, Euclid, Aristotle and Ptolemy, were little concerned with the practical applications of their theories, yet they paved the way for Copernicus, Descartes, Galileo and Newton, who came many centuries later.

The pupil of Euclid who asked "What do I get for learning these things?" typified a state of mind common to all ages, and probably approaching its highest peak in our own time, as indicated by the general apathy with regard to the underpaid members of the teaching profession, and the attitude of the average school pupil or college student who aims not at perfection in his work but sets his goal at the minimum passing grade.

In Francis Bacon's classification of human knowledge (1630) speculative Philosophy occupied a larger proportion of the diagrammatic scheme than would be accorded it by one who attempted a similar outline today, and yet the worker in pure research, or the one who discovers and records an abstract scientific principle, may be conferring upon future generations blessings incalculable.

The continuity of scientific effort in any single direction is more evident in our era than at any previous time in the world's history.

More than two thousand years elapsed between the crude steam appliances of Ctesibus and Hero, and the steam engine of James Watt, and outside of one experiment of Leonardo de Vinci, most of the developmental work occurred in the century in which Watt himself lived.

It took comparatively few years for the discovery of the Hertzian waves to find their practical application by Marconi, and yet Hertz and his co-workers never dreamed of such a thing as wireless telegraphy, nor profited by their work except in reputation.

The work of Albert Einstein, which deals particularly with space and time, and which concerns itself in reality with a method of interpretation of old rather than the promulgation of new principles, is looked upon as epoch-making in its possibilities by some of the mathematicians, physicists and philosophers, who are in close enough touch with the subject to be able to judge thereof intelligently.

For the individual not actively engaged in the fields of work most directly affected by Einstein's observations, articles have appeared; lectures have been delivered and books have been written for the purpose of stopping down the high voltage of the original communication to a lower potential which will not burn out the mental coils and fuses of the average intellect. Dr. Leffmann has humorously and approximately correctly translated the Einstein idea into the epigrammatic form that: "You cannot tell where you are unless you know what time it is and you cannot tell what time it is unless you know where you are."

In Euclidean geometry, as taught in our elementary schools, descriptions of events in space presuppose the existence of a rigid or invariable body to which such events may be referred.

No cognizance is taken of differences of values in observation due to the fact that one observer is in motion while the other is at rest, nor of differences in interpretation due to time discrepancies.

In physical science data have long been accumulating for which no use could be found in the calculations of three dimensional or ordinary space. By the introduction of the time factor a four dimensional space-time combination becomes possible and these hitherto unused data are said to find a place.

In the Einstein method of interpreting mathematical and physical data the length of a measuring unit or the duration of an event

are not absolute quantities, as has always been hitherto assumed in physics, but it is declared that they actually have different values for different systems of reference moving with relation to one another.

Newton had established concepts of what it has been customary to call "Absolute true and mathematical time" and "absolute space."

Experiments of certain physicists had proved man's inability to detect absolute motion (motion with respect to the hypothetical æther). This has recently led to the development of a theorem to the effect that "all laws of physical nature should have been formulated with reference to a definite coördinate system, are valid, in precisely the same form when referred to another coördinate system which is in uniform rectilinear motion with respect to the first."

This empirical law is Einstein's "Special Theory of Relativity."

It is a simple matter to make time duration calculations with a clock situated where the event is taking place. It is more difficult to make such calculations with events happening at two different places, for then some elaborate precautions must be taken to bring the two clocks into synchronous agreement. When we come to deal with calculations where the clocks are not at rest with reference to each other, as for instance, when one is on a railway train traveling at a high rate of speed, all ordinary methods of measurement and comparison fail.

Such refinements of observation seem to be beyond our conceptions of practicality and yet we are assured of their value by those who deal with calculations involving the physical laws, particularly with reference to light.

One of the modern concepts, which is at variance with Newtonian principles, is the declaration that a gravitational field has an influence upon a ray of light. Einstein asserted his ability to prove this by the application of his method to observations and calculations of certain astronomical phenomena. This assertion is said to have been confirmed by observations of the photographic registrations of stars during the eclipse of the sun in May, 1919, and afford justification for the hope that some of the obscure laws of nature may be fathomed by a further pursuit of this subject by those

philosophers who are equipped for this recondite branch of human study.

In the words of one of the recent interpreters of Einstein to the multitude this thought is expressed as follows: "The main philosophic achievement of the special theory of relativity is probably the recognition that the description of the event, which is admittedly only perfect, if both the space and time coördinates are specified, will vary according to the relative motion of the observer; that it is impossible to say, for instance, whether the interval separating two events is so many centimeters and so many seconds, but that this interval may be split up into length and time in different ways, which depend upon the observer who is describing it."\*

The "general theory of relativity" concerns itself with the broader fields of human speculation and endeavor. This is much more daring and less easily comprehended without a knowledge of higher mathematics and there are those among the physicists and mathematicians who characterize it as "Metaphysical Mathematics" and "Intellectual Moonshine."

The fundamental question, "are space and time real?" cannot be answered simply and categorically. Space and time for human comprehension and appreciation are dependent upon the existence of things which lie closer to our senses.

If there were no material bodies we could have no conception of "space" and if no events or changes took place "time" would be devoid of meaning. The world-old question as to what constitutes reality finds the answer of the modern physicist eminently satisfying. "Whatever can be measured is real."

Are space and time real? Both being measurable we unhesitatingly reply in the affirmative. Yet if we perform the imaginary experiment of the celebrated French mathematician Poincaré and "suppose that all material bodies should increase over night one hundred fold," we should be unable to perceive the change, for all of our measurement standards and units would have changed likewise. We should still call an inch by that name although it had increased to more than eight feet. How can we argue convincingly about the reality of space, therefore, except as a relative concept.

So in the same way our time determinations become as closely associated with physical bodies as our ideas of space, and quantita-

\* "Space and Time in Contemporary Physics," by Moritz Schlick.

tive determinations are predicated upon some prearranged method of synchronizing our clocks; otherwise conceptions of simultaneity and equal duration can have no definite and invariable meaning.

The influence of the gravitational field prevents the application of the special theory of relativity to any but systems at rest or moving uniformly and rectilinearly.

The mathematical development of the theory presupposes the introduction of the time factor as a fourth coördinate and calling the new and complex curve thus produced the *World-line* of a given point. The final formulation of the Einstein Law is expressed as follows: "The world-line of a material point is a geodetic line in the space time continuum." The time factor is not introduced simply as such, but as  $ct = x_4$  in which  $c$  denotes the velocity of light.

The statement that every motion is relative may be looked upon as another way of expressing the view that space and time have no physical objectivity. Space and time are not measurable in the abstract. They constitute the framework which we fill up with physical events, both spatial and chronological.

We gain our knowledge of both space and time by direct experience, so in our everyday life we shall continue to deal with them as heretofore. To the physicist and astronomer, however, new fields of research are already opening and it is not too much to expect the future to bring us into closer harmony and a more nearly correct understanding of electrodynamics and gravitational law with a realization, perhaps, that matter after all is but one of the manifestations of energy.

One comfort for the average student of mathematics is found in the assertion that "Euclidean geometry is to remain valid for infinitely small portions" which includes those within the ken of our ordinary daily life. The trouble with the whole subject at present lies in the fact that Einstein enthusiasts are presuming to "prove the unprovable" and to make assertions to the effect that there is such a thing as "finite space without boundaries."

Students of philosophy who remember the speculations of Kant in his "Subjectivity of Time and Space" and Locke in his "Essay on Human Understanding," and Leibnitz, the originator of differential calculus, will enjoy the spiritual exhilaration of cleaning out the cobwebs of the mental attic, by reading one of the works which have recently been published in which the subject is discussed with a

minimum of complex mathematical details, although it will be realized that workers in Physics are rapidly ascending to heights in which the rarefaction of the mental atmosphere will soon make it impossible for the person of ordinary education to accompany them, and in which they will be invisible to those below the cloud strata of higher mathematical formulas.

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## A HIGHER DEGREE IN PHARMACY.

BY JAMES F. COUCH.

Pharmacy has never been more in need of research work upon strictly pharmaceutical problems than it is at the present time. The great stimulus to investigation which was the joint effect of the altered economic conditions caused by the civil war and the direct efforts of the American Pharmaceutical Association and which developed Squibb, Maisch, Lloyd, Hallberg, Remington, Diehl and others reached its peak in 1885 and has been declining ever since. Today we have little beside pharmacological and phytochemical studies in pharmaceutical literature; the problems of pharmacy are left unattacked and unsolved.

What has become of the spirited discussions over the preservation of fluid extracts and tinctures which were wont to absorb the attention of the "scientific section" of bygone years? The problem is still with us for our galenicals still precipitate. Has the interest in this strictly pharmaceutical question disappeared since the corner druggist scrapped his percolator and began to purchase his galenicals from the manufacturing pharmacist?

What has become of the perennial attempts to compound a strong solution of Epsom salt with the taste so disguised that the objection to this valuable medicament might be largely overcome? The solution of this problem would be a boon to pharmacist, physician, and a long-suffering general public. The pecuniary reward to the discoverer, if he chose to market his preparation as a semi-proprietary, would be considerable. And this problem is not at all unsolvable. While it may not be quite as simple as the debittering of cascara it needs only determination and study to ensure success.

Many problems have been partially or fully solved by manufacturers. In most cases, however, the results of such investigations and the processes devised are withheld from publication and,

consequently, diffuse very slowly and imperfectly into the general knowledge. It is not my purpose here to attack the "trade secret" doctrine; there are many arguments which support it; the net effect of it is, as most will acknowledge, an impediment to pharmaceutical progress and actual loss to the secretive ones themselves.

For progress in the solution of our problems, then, we must look to two sources, the independent investigators and the colleges of pharmacy. Of the first class the numbers are small, so small that main reliance must be placed upon the second class, the colleges.

From these latter there has emanated a varying stream of investigations covering the whole field of pharmaceutical sciences. At times the number of reports published has been very large; at other times it has dwindled to quite inconsiderable volume. It needs a stimulus and the following paper offers a suggestion as to how this stimulus may be found and applied.

It is proposed that there be established the degree of Doctor of Philosophy in Pharmacy.

In other lines of scientific activity a large proportion of the research work accomplished is done at our colleges by students who are candidates for the Ph.D. degree. The research professor has a constant stream of students coming to him to be put to work on some of his problems. He may carry out investigations covering a long period of years and utilizing a number of students. The result of this system has been the accumulation of vast amounts of eminently practical knowledge and the dispelling of moss-covered and age-encrusted errors. The student acquires a mastery of his subject, a finished technique, and the very desirable degree without which certain avenues of scientific endeavor are all but closed to him.

Can this not be applied to pharmacy? Let us see. The standard requirements for the Ph.D. degree in American institutions of the first grade are; the bachelor's degree from a college of good standing; a knowledge of German and French; and three years' graduate work, including research, at least one year of which must be spent in residence at the university which grants the degree. The graduate work involves the accomplishment of a stated amount of work in one "major" and two "minor" subjects with the presentation and defense of a thesis which reports the results of original investigations conducted on problems in the "major" subject. Original work

in the "minor" subjects may also be presented but is not usually required.

In order to obtain adequate recognition for the Ph.D. in Pharmacy these standards must be rigidly adhered to. If the degree should be granted to candidates who could not fulfill these requirements the result would inevitably be a cheapening of it with consequent disrepute and the circumstance would react very unfavorably upon pharmacy.

As applied to the art of pharmacy the requirements should include a certain amount of "practical" experience and it is permissible that a small amount of credit be given for unusual or extensive qualifications of this sort. Credit may be given for research work conducted in and published from industrial laboratories and it is desirable that this be done. In this way the time required to obtain the degree may be somewhat shortened. As the major subject of the candidate, "pharmacy" should always be chosen; the minors may be selected from the long list of pharmaceutical sciences and one minor may also be "pharmacy."

In addition it would become possible for any college of pharmacy which grants the higher degree to confer it *honoris causa* upon eminent pharmacists whom it desires to honor. The possibility of being so honored would furnish an additional stimulus to independent investigators.

The effect on general pharmacy of the establishment of this degree must be widespread and must extend far beyond the stimulation of research and solution of problems. It will serve to draw a distinction between the man who studies pharmacy merely for the purpose of passing the State board examination and the real pharmacist who desires a profound knowledge of pharmacy and of the sciences germane to it. Eventually the faculties of our colleges will be composed of Ph.D. (Pharm.) men and the same type of men will be found in charge of the manufacturing, control and research laboratories of our pharmaceutical factories. A general rise in the whole tone of the art of pharmacy must follow for these men can demand and will receive the recognition accorded to first-rate technical experts. The military and naval services could no longer withhold commissions from pharmacists when the candidates possessed such qualifications.

The career open to a pharmacist of this grade would unquestionably attract young men of superior abilities and high aims who



now enter other fields which return greater rewards than does pharmacy. What a raising in standard would follow the influx of a proper proportion of the best of the intellectual youth in the country! Is it not well worth attracting?

All that need be done to start is this: let one of our prominent colleges of pharmacy announce that it will confer the Ph.D. (Pharm.) degree upon properly qualified candidates who comply with certain stated requirements. If necessary, the college may obtain from the State the right to confer the degree. At first the number of candidates will probably not be great but, as time goes on and when men observe that the holders of the degree are preferred for the better sort of pharmaceutical positions, the number of candidates will increase until the degree will come to be accepted as a prerequisite for a scientific or technical career in pharmacy.

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#### HYENANCHIN AND OTHER CONSTITUENTS OF *HYENANCHE GLOBOSA.*

A paper on this subject was read by Dr. T. A. Henry, Director of the Wellcome Chemical Research Laboratories, at the meeting of the Chemical Society of London on December 2. This plant belongs to the natural order Euphorbiaceae and occurs in South Africa, where it is used for poisoning wild animals, especially hyenas, a use reflected in the generic name *Hyenanche*, and also in the common name of the plant, hyena-poison. It was examined in 1858 by Henkel and in 1892 by Engelhardt, and shown to contain a toxic substance, which the latter author isolated in crystalline form and called hyenanchin. It is now shown that the crude crystalline material isolated from the plant consists of two isomeric crystalline substances of the formula  $C_{15}H_{18}O_7$ ; one of these is toxic and for this the name hyenanchin is retained, whilst the other, which is physiologically inactive, it is proposed to call *isohyenanchin*. Pharmacological investigation of these two substances is still in progress by Dr. J. Trevan of the Wellcome Physiological Research Laboratories but sufficient has been done to show that hyenanchin has an action, weaker than, but identical in kind with that of picrotoxinin and so belongs to the group of non-nitrogenous, convulsant poisons. It is interesting in this connec-

tion to note that just as hyenanchin occurs along with the non-toxic isomeride, picrotoxinin is associated in *cocculus indicus* with the inactive substance picrotin. All four substances are dilactones and whilst picrotoxinin and its associate yield acetone on distillation with alkalis, hyenchanin and its isomeride yield hydroxyacetone.

The subsidiary components of Hyenanche include a new wax alcohol  $C_{24}H_{49}OH$ , a new phytosterol  $C_{28}H_{46}O$  and a new yellow colouring matter  $C_{15}H_{12}O_6$  belonging to the flavone series and showing some characteristics in common with morin.

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## THE TRADE-MARK ACT OF 1920.

By L. M. MIDA

of

Mida's Trade-Mark Bureau,  
Chicago.

Help in holding business already won and in gaining new patronage is given manufacturers and exporters by the trade-mark law of 1920.

Before the passage of this law, there were trade-marks in use which could not be registered under the Trade-Mark Act of February 20, 1905.

That is to say, although the validity of such trade-marks was acknowledged in common law, they did not meet the requirements of the United States Patent Office.

In many instances, such trade-marks earned their popularity at first in local circles of trade. They served to identify a product in the community where it was made and sold.

When devising these emblems, manufacturers had in mind some symbol which would not be hard to remember. Moreover, they sought to compose a token which would be different enough from other trade-marks to enable people easily to recognize the goods to which it was applied.

Not much thought was spent upon whether or not the trade-mark could obtain registration in the Patent Office at Washington, D. C.

There were numerous cases in which a time came when the

manufacturer achieved national distribution of his product under the local-trade-mark and began to plan for business in foreign markets.

Then he discovered that his trade-mark could not get official recognition abroad because some foreign countries require certificates of United States registration before granting similar rights under their laws.

The new Trade-Mark Act of 1920 removes this obstacle from scores of trade-marks which have hitherto been valid only in common law.

A notable example is that of "Kitchen Klenzer," which was refused registration under the law of 1905 because it is descriptive in character.

### **KITCHEN KLENZER**

The manufacturers of Kitchen Klenzer had spent a fortune in advertising that name. When they were refused registration for it under the law of 1905, they appealed to the Commissioner of Patents.

The latter could legally pursue only one course in the matter. He was obliged to confirm the Examiner of Trade-Marks in his decision that this mark was descriptive and, consequently, barred from registration under the provisions of the law.

The new Trade-Mark Act of 1920 permits registration of descriptive or geographical words and names of persons, firms, or corporations, without requiring that they be displayed in some peculiar or distinctive manner.

Certain reasonable restrictions, however, remain in effect, forbidding registration of trade-marks consisting of immoral or scandalous matter or comprising the flag or coat of arms or other insignia of the United States or any simulation thereof, or of any state or municipality or of any foreign nation, or of any design or picture which has been or may hereafter be adopted by any fraternal society as its emblem, or of any name, distinguishing mark, character, emblem, colors, flag, or banner adopted and publicly used by any institution, organization, club, or society which was incorporated in any State in the United States prior to the date of the adoption and use by the applicant.

Thus the Trade-Mark Act of 1920 does not exclude marks which are merely geographical, as for example the word "Cleveland," which has become widely known in connection with a line of tractors.

## *Cleveland*

This trade-mark represents big values in the form of good will, resulting from persistent publicity and its logical accompaniment, good craftsmanship and uniform quality.

It was refused registration under the law of 1905, but has been granted Federal recognition under the more liberal provisions of the Trade-Mark Act of 1920.

Other marks, descriptive in character, were rejected under the old law for the reason that they consisted principally of a representation of the goods upon which they were used.

A case in point is that of a picture of a pair of children's garters, employed as a trade-mark for garters.

It is true that a measure of relief was granted by the Act of 1905 in its "ten-year" proviso, which permitted the registration of a common-law mark which had been in exclusive use by the applicant for ten years preceding February 20, 1905.

But it made no arrangement for the protection of common-law marks which were adopted at any time after February 20, 1905, or which might be adopted at any time in the future.

In the circumstances prevailing prior to the passage of the Trade-Mark Act of 1920, any of the common-law trade emblems—as, for example, "Kitchen Klenzer"—could be stolen outright by a citizen of another country and registered in that country as his exclusive property.

The American owner of the trade-mark could not prevent the theft because he could show no certificate of Federal registration to enable him to forestall such action by obtaining registration of the trade-mark in his own name in the foreign country.

Unless he took the time and trouble to devise a new trade-mark, wholly different from the stolen one, he would have to pay tribute to the citizen of another land for the right to import and sell his goods in that land under an established trade-mark which was his in the first instance.

In the hearings conducted by the House Committee on Patents,

prior to the enactment of the 1920 Trade-Mark law, Commissioner of Patents Newton drew attention to the ease with which well-known American trade-marks are pirated in some foreign countries.

He told of an experience of the Eagle Pencil Company. This company has its trade-mark, the word "Eagle" with a picture of an eagle, registered all over the world.

The company shipped some of its pencils to one of the South American countries before registering its trade-mark there.

A man who knew the good will value of the company's emblem had gone to that country and registered the trade-mark for himself.

When the Eagle Pencil Company's cargo of pencils arrived, it was confiscated. Under the trade-mark laws of various lands, no trade-mark which is an infringement of a trade-mark already registered in the country is allowed to pass the customs. For more than twenty years, the Eagle Pencil Company was in litigation over the matter without gaining the slightest degree of redress.

Frequently, the good will betokened by a trade-mark—and often inseparable from it—is estimated in terms of millions of dollars.

Although the Trade-Mark Act of 1920 affords legal protection for the good will embodied in a trade-mark and opens the way to foreign registration thereof, it is beyond the province of the act to stop the turning of domestic good will into ridicule or gibberish or ill will in a foreign market.

In other words, a trade emblem which is graphic and persuasive in this country may be obscure, repellent, or a laughing stock in another country. This may come to pass as a consequence of difference of language or clash of racial custom or religious beliefs. For example, in the tailoring industry there is a prosperous American firm bearing the name of "Bobo and Company." It is conceivable that this firm might want to use the name "Bobo" as a trade-mark for its goods in Latin America. No difficulty would be encountered in securing Federal registration for the name in this country after it had been used in interstate commerce for one year. Nevertheless, it would not be advisable to register the name as a trade-mark in any of the Spanish-speaking republics, because "Bobo" in Spanish means dunce, dolt, fool, simpleton.

Furthermore, a particular trade-mark may be free from everything which would militate against its prestige in foreign markets

and yet be so designed as to be denied registration in another land.

This may happen when the trade-mark is so composed that its units are not intimately blended. A citizen of the foreign country may obtain registration for himself of the several distinct parts of such a trade-mark and thus prevent the use of the composite trade-mark—except upon payment of blackmail to him.

It is apparent, therefore, that American manufacturers who wish to sell their goods in foreign markets need something more than legal protection for their trade-marks. They require the knowledge and services of a competent agency to make a study of the trade-mark with reference to its fitness for general use in export business and to find out first and foremost whether or not it sufficiently meets the requirements for ample protection in this country. The practice of relying upon common-law rights is robbed of much of its former excuse now that the Patent Office has opened the door to registration of practically all "common-law" marks.

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## ABSTRACTED AND REPRINTED ARTICLES

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### ELDRIN, A NEW PLANT CONSTITUENT.\*

By JOHN URI LLOYD, PH.M.

CINCINNATI, OHIO.

For thirty or forty years in the experiments I have made with drugs, plants and plant structures, I have met continuously the fact that linked with each plant texture there was something present that under the influence of an alkali gave a yellow color. For example, strip a paw-paw of its bark and touch the white inner surface with a solution of potash—now it turns yellow. There is probably one rule in this as elsewhere, and that is the rule of exceptions. I hope to find one white blossom that will not turn yellow. If I do, the exception may be of help to the botanist, for it may be the forerunner of a class distinction.

\* Portion of an address on Plant Constituents delivered at the meeting of the Ohio State Eclectic Medical Assoc., May 18, 19, 20, 1920; reprinted from the *Eclectic Medical Journal*, Dec., 1920.

For years this yellow phenomenon was before me, but I could not catch the material that produced it. About a year and a half ago I decided that if I isolated this yellow something that pervaded all plant tissues so linked with impurities as seemingly to defy isolation, it must be obtained from something that is white, something that does not carry a mass of extraneous material to contaminate the principle desired. Then it occurred, why not use the petals of a *white* flower to get this *yellow* something?

The elder was then in bloom. These, I found, turned deep yellow with ammonia gas. I procured fifty pounds of elder flowers, put them in a percolator, made a tincture, and worked it by means of neutral solvents and excluders, to rid the product of the alcohol, chlorophyl and wax. I had five gallons of the chlorophyl-free liquid, and said to Mr. Miller, who was assisting me: "Place the jar in a cold situation, and tomorrow morning I shall examine it." Next morning I tipped the jar very carefully, and all down the sides were little white concretions about the size of pin heads. It was the thing I have been seeking forty years.

I took one of those pin heads to the laboratory and dropped it into distilled water and it did not dissolve. I added ammonia—behold! it immediately dissolved, the liquid turning deep yellow. It was only the size of a pin head, but there were thousands of them. And they kept increasing in size. The marvelous phase of this subject is, I got eleven ounces (crude) of that substance out of that fifty pounds of elder flowers. Before that, by reason of faulty research, I could not get a grain from anything.

The first thought of a pharmacist is, what value a new substance may have in medicine. Alas, the greater part of my work has been the repeated finding of something that had no value. I sent some of this material to Prof. R. Adams Dutcher, University of Minnesota, requesting that he make a physiological examination of it. His preliminary report was to the effect that, according to a preliminary investigation, it had no physiological action. May I not ask, should a peculiarity of action be expected of a substance pervading plant tissues everywhere?<sup>1</sup>

In this cylinder I have distilled water, and I propose to put

<sup>1</sup> I had vitamins in mind, there was reason to hope that a general life supporter of plant life, serviceable to animals, could be found and isolated. Not a poison of energetic action. This, I accept, Dr. Dutcher demonstrated as a fallacy in the direction of this substance.

into the water a small amount of this material. Note that it settles to the bottom. It is perfectly insoluble. One grain shaken with a gallon of water apparently disappears, but if let stand until the next day, behold, it is all at the bottom. I now shake the mixture, and pour half of it into another cylinder, then add a little ammonia waer—note the change in color, to deep yellow. A very delicate reagent is it for an alkali. Let us now make both liquids yellow. Into one I pour diluted sulphuric acid, in excess, to destroy the ammonia. The liquid becomes colorless.

Now the question came to me, "Why is the white flower white when it has the yellow material in it in such quantity?" Then I figured to myself it must be because the white petals carry also an acid which in contact with the yellow material makes it white. In other words, would the white flower be yellow if there was an alkali in the petal instead of an acid? Crushing the flower in a mortar with a little distilled water gave a sharp acid reaction. Blue litmus turned red at once. The acid was present.

The question arises, What is the use of this thing in nature? I think I comprehend the subject, but it is too great to try to bring before you today.

I am going to ask you to be charitable in what I have said concerning the theories I now hold. I may be right and I may be wrong. We can see this color change and we know that the petals hold organic acid. What of it? I don't claim that anything I have brought is new; quite the contrary. So far as I know, this experiment has not been made. In some literature unbeknown to me it may be explained. It doesn't matter whether it is new or old—it is a phase in plant economy that is a fact, and may be of service other than as a medicine.

I asked myself, Why the material could not be used to make a test paper? Why would not paper saturated with a solution of this material turn yellow with alkali and colorless with acid? I tried it and it worked. There is a shade between red and blue litmus which makes it difficult sometimes to quite determine the end-reaction. There is no intermediate shade with this.

*For example*, let us now pour into these tumblers some water, and into the one put some ammonia and in the other dilute sulphuric acid. The paper I hold in my hand has been saturated with a weak solution of this material and dried. I dip it into the acid.



See, it is colorless. Now I dip it into the ammonia; it instantly turns yellow.

You ask the name of this material. I call it *Eldrin*. But it may have been long known elsewhere and recorded under a different name or different terms.

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### CHAULMOOGRA OIL DERIVATIVES.\*

Chaulmoogra oil is one of the few members of the group of fatty oils which are believed to have distinct physiological effects outside of their nutritive value. The fatty oils are of great physiological importance, but, heretofore, chiefly in relation to nutrition and the general metabolism of the body. In a series of papers from the Wellcome Research Laboratory, by Power and his collaborators, the constitution of chaulmoogra oil and some of the closely related oils was elucidated. They discovered a new series of fatty acids represented by two members—chaulmoogric acid,  $C_{18}H_{32}O_2$ , and hydnocarpic acid,  $C_{16}H_{28}O_2$ . These acids differ from any other known fatty acids in that they rotate the plane of polarized light to a notable degree—chaulmoogric acid  $(\alpha)_d = +62.1^\circ$  and hydnocarpic acid  $(\alpha)_d = +68^\circ$ . The studies on their constitution indicated that each of these acids contains a five-carbon-ring nucleus. Both of these acids were isolated from chaulmoogra oil derived from the seeds of *Taraktogenos kurzii*, and also from the oil of closely related species belonging to the genus *Hydnocarpus*. Power and his co-workers did not concern themselves with the therapeutic use of chaulmoogra oil.

It would appear possible that the distinctive action of chaulmoogra oil, as heretofore reported, may be due either to the glycerides of the unique fatty acids of chaulmoogra oil or to the presence of some other oil-soluble constituent not a glyceride. The first step in the attempt to identify the active agents would be the separating of chaulmoogra oil into fractions and the use of these fractions on groups of lepers. The separating of the glyceride mixtures which make up the various vegetable fatty oils is very difficult; the fatty

\* Abstract from Public Health Reports, Volume 35, No. 34, the United States Public Health Service, prepared by Joseph W. England.

acids obtained by the decomposition of the glycerides are somewhat more readily separated.

Sir Leonard Rogers, in his experiments using the intravenous injections of the sodium salts of the acids derived from chaulmoogra oil, made use of fractions, separated by Ghosh. The data presented by Ghosh showed clearly that he was dealing with mixtures of fatty acids, and probably very complicated mixtures. The separation of the constituent fatty acids from the mixed product derived from the saponification of chaulmoogra oil by means of fractional crystallization is a tedious and complicated task, and Ghosh did not meet with much success.

It is quite clear from the results heretofore published that although there is a therapeutic agent (or agents) in chaulmoogra oil of marked value in leprosy, none of the attempts to isolate or identify this agent has led to conclusive results.

A recent publication of Sir Leonard Rogers describes the use of "gynocardate of soda" and "morrhuate of soda." His term "morrhuate of soda" refers to the sodium soaps of the fatty acids of cod liver oil, and he reports excellent results from the intravenous and hypodermic injections of this material. The fatty acids of cod liver oil are of a peculiar and unusual type, although not of the chaulmoogric series. If the results of Rogers are confirmed, it will appear that the fatty acids of cod liver oil are also useful in leprosy. Although it may be, as suggested by Rogers, that "other unsaturated fatty acids may also be expected to yield effective preparations against the acid-fast bacilli of both leprosy and tuberculosis," it seems to us unlikely that this is a property common to all unsaturated fatty acids. For example, oleic acid, which is unsaturated to the same extent as chaulmoogric acid, is a common body constituent, and it would therefore be rather improbable that weekly injections of, say 5 Cc. of a 3 per cent. solution of sodium oleate amounting to 0.15 gram dry material, would have any such effect in leprosy as has been reported following the use of even smaller quantities of the sodium soaps of the fatty acids of chaulmoogra oil. Obviously a wide and important field for chemical and physiological investigation has been opened by this work of Sir Leonard Rogers and our own work here.

As an initial step, the fatty acids of chaulmoogra oil were separated into four fractions in the chemical laboratory of the College of Hawaii. One of these fractions was chaulmoogric acid and the

other three were mixtures of acids having somewhat different properties. These fatty acid fractions are solids, and therefore unavailable directly for hypodermic or intramuscular injections. One of the first problems was to find a suitable form of material for injection which would allow rapid absorption into the circulation. It was found that the ethyl esters of the fatty acids were thin fluid oils lending themselves readily to intramuscular injections and were readily absorbed.

The four fractions originally tried out, and designed, respectively, "A," "B," "C" and "D" were of the following character:

Fraction "A": The ethyl ester of chaulmoogric acid.

Fraction "B": The ethyl esters of the other fatty acids readily separating on cooling the alcoholic solution of the mixed fatty acids of chaulmoogra oil, doubtless containing considerable of "A."

Fraction "C": The ethyl esters of the fatty acids remaining in the mother liquor from the separation of the acids in "A" and "B" and yielding lead salts readily soluble in ether.

Fraction "D": Ethyl esters of the fatty acids accompanying "C" in the alcoholic separation, but yielding lead salts not readily soluble in ether.

The early results of the use of these fractions "A," "B," "C," and "D," together with some details of the methods of their preparation, are given by Hollmann and Dean.

The results published and a continuation of the same line of work led to the general conclusion that the therapeutic agent in chaulmoogra oil is able to survive the chemical treatments involved in the making of these preparations and is itself distributed through all four of the fractions. The differences in results, using the different fractions, are not sufficient to warrant any final conclusions regarding their relative efficiency; patients receiving each of the fractions have shown marked improvement, have become bacterially negative, and have been paroled. It is impossible, however, to draw definite conclusions from this work because of the fact that all patients who received the injections also regularly received chaulmoogra oil by mouth in substantial quantities. We cannot say therefore, whether the beneficial action in any particular case is due to the material injected or to the combined action of the material injected and that taken by mouth. The general observation that Chaulmoogra oil taken by mouth has a beneficial but not decisive action lends color to the belief that the most important factor in

the improvement of the various cases is the injected material. As a series of experiments intended to develop the best method for leprosy treatment the plan followed was satisfactory, but it is not satisfactory as a method of demonstrating the relative efficiency of different fractions of the oil.

#### DISTILLED ESTERS.

As already indicated, the processes which resulted in the fractions "A," "B," "C," and "D" are of such a character as to make it improbable that any other material except fatty acids would survive them and be distributed in all four of these fractions. Still further evidence on this point was gained by a different system of fractionation. In this case the mixed fatty acids derived from the saponification of chaulmoogra oil were converted into ethyl esters by heating with absolute alcohol in the presence of dry hydrochloric acid gas, giving a mixture of the ethyl esters of all the acids present in the crude oil. This acid mixture was distilled in vacuo at a pressure of 30 to 34 mm. The distillate was cut into three fractions of different boiling ranges, designated "E," "F" and "G." These distilled esters are colorless liquids. At the time the first work of this character was done no apparatus was available to provide higher vacua and allow satisfactory distillations. The fractions "E," "F" and "G," were used for intramuscular injections in a number of patients, beginning in January, 1919, and in some cases extending until about the 1st of July of that year. It was found that all the cases receiving each one of the fractions "E," "F" and "G" showed improvement—some of them quite rapid—indicating that the methods employed in their production had not resulted in the destruction of the therapeutic agent or agents.

The same uncertainty surrounds the interpretation of these results as exists in the cases receiving fractions "A," "B," "C" and "D" since all were getting chaulmoogra oil in capsules three times daily in addition to the weekly injections. We can say, however, that whatever virtue resides in the use of chaulmoogra oil derivatives injected intramuscularly in combination with the oral administration, that virtue is probably not lost or segregated to an appreciable extent by any of the chemical or physical conditions to which these various preparations have been exposed.

The use of vacuum distillation as a means of separating the esters of the fatty acids and the fatty acids themselves is receiving extensive application in the further chemical investigations now in progress.

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## ON THE USE OF POKE ROOT IN MEDICINE.\*

BY E. M. HOLMES, F.L.S.

My attention was recently directed to the use of this plant in cancer of the breast, and on looking up the statements concerning it, I have been surprised to find how vague the therapeutic action of the drug appears to be, and how little is known of its active principles. Squire, in the "Companion to the British Pharmacopœia," states that in large doses it is emetic, purgative, and slightly narcotic. Martindale, in the 17th edition, 1920, of the "Extra Pharmacopœia," ascribes emetic, cathartic, and alterative properties to it, and refers briefly to its use for painful mammae. In the "Year-Book of Pharmacy, 1896," p. 120, a quotation from the *Med. Chim.*, n.s. III, p. 288, is given, in which a Dr. Goodman states that he has obtained very good results in the treatment of epithelioma, with fresh leaves of the plant applied in the form of a plaster. The application is said to be painful but quite free from danger, and exercises a very marked destructive action on the morbid tissues. Stillé and Maisch ("National Dispensatory," 4th edition, p. 1154), state that the most probable evidence in favor of the medicinal powers of the plant relate to its use in rheumatism and diseases of the skin; and mention is also made of the alleged statement that it prevents and relieves mammary inflammation after delivery; and also that, according to Rutherford, the resin is a powerful hepatic stimulant.

In a homœopathic work by E. H. Ruddock (1879), entitled "Homœopathic Vade Mecum," it is described as a remedy for inflammation, swelling; hardness, and morbid sensitiveness of the breast, also for boils; and in a footnote it is stated that the plant is in constant use in the dairies of America to disperse caking, or inflammatory enlargements of the udders of cows, and that it has

\*From *The Pharm. Jour. and Pharmacist*, Nov. 6, 1920.

been most successfully\* used in the human female, even after supuration of the gland has set in and sinuses have been formed.

That *Phytolacca decandra* possesses active properties there can be no doubt, and its physiological action and its chemical constituents seem worthy of careful investigation. Trimble, in *Amer. Jour. Pharm.*, June, 1893, obtained from the root a constituent which appeared to be a saponin with acid properties, as it caused much frothing when shaken with water, was precipitated from alkaline solution by dilute sulphuric acid, and acted as a sternutatory. Four years later G. B. Frankforter and F. Ramaley (*Amer. Jour. Pharmacy*, 1897, pp. 281-290) found in the root about 1 per cent. of a resin, an acid, combined and free, calculated as formic acid, and obtained indications of the presence of an alkaloid, existing as a salt as well as in the basic condition. An English wholesale herbalist tells me that herbalists regularly send to him for the fresh root, which they sell as a remedy for tumors and cancer of the breast, and that a lady who is the daughter of a veterinary surgeon has a regular practice in the treatment of tumors with poke root, and that he himself has given it to persons suffering with swelling and tumors with the happiest results. He has used the fresh root in the form of a poultice, kept wet with the tincture, and covered with oiled silk, till a good crop of pustular sores are produced, when the tumor will resolve. He is willing to supply the fresh root to any qualified medical practitioner who will give it a fair trial in mammary cancer. There seems to be sufficient evidence that the root, besides possessing emetic, cathartic, and cholagogue properties, acts as a discutient for tumors. That it deserves a careful investigation as to its chemical constituents is evident from the way in which they act, especially the saponin, which may possess special haemolytic actions. Any remedy which promises the possibility of relief for any form of cancer is certainly worthy of trial.

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#### THE CULTIVATION OF BUCHU.\*

The cultivation of buchu in South Africa is dealt with in the *Imperial Institute Bulletin* (Vol. xvii, No. 4), in the course of which the measures taken to prevent the wholesale destruction of

\* From *The Chemist and Druggist*, Nov. 13, 1920.

the plants is indicated, similar information having been given in this journal from time to time. Although these measures will doubtless help to preserve the wild plants from extermination, there is no question that the best way to obtain a continuous and regular supply of the leaves is by cultivating the plants. A further advantage of cultivation is that it would ensure the leaves being marketed in a pure state. At present the three standard forms of buchu are sometimes found to be adulterated with leaves of other species of *Barosma*, while those of *Empleurum serrulatum* are occasionally present in considerable quantities in parcels of long buchu (*B. serratifolia*). Cultivation experiments with buchu have been made from time to time by private persons (see, for example, *Agric. Jour. Union of S. Africa*, 6:80, 1913), and more recently experiments with *B. betulina* have been conducted at the National Botanic Gardens, Kirstenbosch, particulars of which are given in the *South African Journal of Industries* 2: 748, 1919. From this account it appears that seed was sown in 1914 in four plots situated in different positions on the slopes of Wynberg Hill. At the base of the slope, where the soil consisted mainly of a black, sandy alluvium, which was occasionally flooded during the winter, only a few seeds germinated at the driest end, and those did not survive the first winter. The best results were obtained on a plot in an open, sunny position well up the slope of the hill. Here the soil was a red, gritty loam, rich in iron and deficient in lime, the sub-soil being dry and consisting of clay containing a large quantity of quartz grit, with here and there a seam of ironstone gravel. In June, 1916, a further sowing was made at this spot in rows four feet apart, the land being trenched and no manure added. About 80 per cent. of the seed germinated in this case, which was much higher than in any previous sowings. The germination, however, was slow. Seed was also sown in tins in a nursery, to supply plants for filling gaps in the plantation, but not more than 20 per cent. germinated. The seed shown *in situ* was not watered, and rain fell on only two days in the first fortnight, whereas the surface soil in the nursery was kept moist by watering. It appears, therefore, that the seed dislikes much moisture during germination. When twelve months old the seedlings were thinned out, and some were transplanted but not more than 10 per cent. succeeded. When two years old the plants sown in 1916 were from twelve to eighteen inches high, very bushy, and some of them flowered and seeded. It is suggested that

the best method of harvesting is to cut the whole plant back to near the crown when 18 months old, and thereafter annually, cutting each season a little above the previous year's cut. By this method a harvest is obtained every year, and the yield should gradually increase. It would be necessary, however, to allow a number of plants to grow on and flower, in order to obtain seed for the renewal or extension of the plantation. The yield of dry leaves from a row of 80 yards long, cut in May, 1918—that is, when the plants were about two years old—was  $8\frac{1}{2}$  lbs. With rows four feet apart this is equivalent to a yield of about 400 lbs. per acre. It is stated that the growth of the plants subsequent to being cut back was entirely satisfactory, and none of them died. The results obtained in the experiments at Kirstenbosch indicate that under suitable conditions the commercial cultivation of buchu should prove a success. *B. betulina*, the most valuable kind, alone should be grown. The plant is particularly adapted to dry conditions, and may be cultivated on sunny hillsides, where other crops will not succeed.

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### THE PROGRESS OF MICROBIOLOGY.\*

In common with all the natural sciences, microbiology passed through an empirical stage. For it is only in mythology that Minerva springs forth a finished product from the brow of Jove. Jenner's discovery of vaccination as a prophylactic for small-pox was an inference from a fact of observation—namely, that persons who had once been infected with cow-pox seemed to enjoy immunity from small-pox. Neither Jenner nor his immediate successors reached any rationale of the process by which this protection is effected. It was not until Pasteur and his school demonstrated the casual relationship between the specific living organisms and disease, that microbiology became entitled to rank as a science, and the ground was clear for the introduction of sero-therapy and vaccine-therapy which have since made such rapid strides as scientific methods for the prevention and cure of disease. According to Metchnikoff's theory of phagocytosis, the white blood corpuscles are engaged in a perpetual campaign against the microbic invaders of the blood-stream, which if not destroyed or rendered innocuous may do dire

\* From *The Pharm. Jour. and Pharmacist*, Sept. 4, 1920.



mischievous to, or bring about the downfall of, the living human body. But there are also elements in the blood-stream which react upon the bacillary and other organic poisons which may be absorbed into it. These elements form the so-called antibodies, which by chemically combining with the virus neutralize it. According to the current theory these antibodies may be reproduced and persist in the blood for an indefinite period. Jenner believed that a single attack of cow-pox or a single vaccination protected the subject for the rest of his life, an expectation falsified even during Jenner's own lifetime. No one can now say for certain how long the protective period lasts. And this uncertainty prevails also as to protection from other diseases for which special vaccines, stock or autogenous are used. If the results of his recent researches are confirmed, Dr. Besredka, of the Pasteur Institute, has made a remarkable discovery which puts an entirely new complexion on the accepted view of immunization. He finds that while the infusion into the blood of the living germ which cause a disease, such as bacillary dysentery, does not, contrary to theory, produce acute general toxæmia, it produces exactly the same effect locally upon the bowels as if the germs had been taken into the system by the mouth. And the result is the same whether the germs are hypodermically or intravenously injected. While a single injection of dead dysentery germs have after a lapse of 18 days increased the amount of antibody 400 times, it was found that after two injections, at an interval of 8 days, the antibody had disappeared from the blood. The inference is that microbes, living or dead, have a selective affinity for certain tissue systems or definite areas in these, and that the protective mechanism is formed not in the blood-stream but locally in the site susceptible to the given disease. Dr. Besredka's experiments show that as regards typhoid, dysentery, paratyphoid, and similar infections, "vaccination is only efficacious when the vaccine finally reaches the intestine or certain zones of it. The mode of vaccination to be preferred is the oral route; it gets to its required position directly and with a maximum of security." Thus administered there is no local irritation, such as sometimes occurs at the site of a hypodermic injection. Both rabbits and mice which swallowed the dead germs were "solidly protected." Some of the lay newspapers in their references to Dr. Besredka's discovery wrongly assumed that vaccination *per se* would be of general application. So that vaccination by the skin against small-

pox is to be superseded by a dose of calf lymph taken by the mouth. But this is going beyond what is written. Dr. Besredka's researches have reference exclusively to localized infections, and it is doubtful whether immunization from diseases of the type of small-pox—which is distinguished by general constitutional disturbance and an eruption all over the body—can be secured by ingestion of vaccine lymph. If Dr. Besredka's conclusions are established they will not invalidate the first principles upon which serotherapy and vaccine-therapy are founded, and his method has the undoubted advantage of simplifying and otherwise improving the technique for the administration of prophylactics—microbic in their nature or origin.

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## BENZYL ALCOHOL FOR TOOTHACHE.<sup>1\*</sup>

By DAVID I. MACHT, M.D.,

BALTIMORE, MD.

In 1918, I<sup>2</sup> announced my discovery of the local anesthetic properties of benzyl alcohol, or phenmethylo, and published both pharmacologic and clinical data on the subject. I found that solutions of that drug in concentrations of from 1 to 4 per cent. by volume, in physiologic sodium chloride solution or in distilled water, furnished a satisfactory local anesthetic for general surgical work, on the one hand, and that benzyl alcohol was at least forty times less toxic than cocaine, on the other. It was found that solutions of phenmethylo produced efficient anesthesia, especially when infiltrated in the tissues, either alone, or, still better, combined with small doses of epinephrine. On application to mucous membranes, solutions of benzyl alcohol produced also a distinct anesthetic effect, but the anesthesia is very superficial and does not penetrate into the deeper layers of the tissues. It was found that a much better anesthesia of mucous or skin surfaces could be produced by application of pure benzyl alcohol. Pure benzyl alcohol cannot be injected

\* From *Jour. Amer. Med. Assoc.*, October 30, 1920.

<sup>1</sup> *Pharmacological Laboratory of the Johns Hopkins University.*

<sup>2</sup> Macht, D. I.: *J. Pharmacol. & Exper. Therap.*, 11: 263 (Apr.) 1918.

into living tissue for the same reason that pure ethyl alcohol cannot be administered in that way: it leads to local necrosis. When applied to mucous surfaces, however, the drug is not irritating and produces a marked anesthetic effect.

I undertook experiments with a view of enhancing the penetrating power of benzyl alcohol when applied to mucous or skin surfaces. It was found that when the drug was mixed with certain lipoid solvents, the local anesthesia after its application extended more deeply below the surface. Among the most satisfactory of such solvents were found to be xylene and chloroform, especially the latter.

In the present note I wish to call the attention of the general practitioner to a very satisfactory minor use of benzyl alcohol. I have found, as have others, that benzyl alcohol either alone (100 per cent.), or, still better, when mixed with an equal part by volume of chloroform, furnishes a most efficient anodyne for toothache, when introduced on a pledget of cotton into a tooth cavity, or applied to an exposed nerve. The relief obtained by the use of such drops is marked and almost instantaneous, and is also long-lasting. I am not aware of any other drug, with the exception of cocaine, which is more efficient in relieving toothache. As benzyl alcohol is the least toxic of all the well-known local anesthetics, the repeated and free use of such a combination as was described above is free from the objections which are raised by the employment of cocaine, and it can be administered with impunity even to small children. It is for this reason that it was deemed worth while to publish this note in order to advise the medical practitioner of a simple remedy for the relief of one of the most excruciating forms of pain.

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#### PIEDMONTESE PEPPERMINT OIL.\*

Next to the essential oils of lemon and orange, that obtained from peppermint enjoys a high reputation among the numerous volatile oils produced by Italy. Sig. Michelletti, the editor of the "Rivista Italiana delle Essenze e Profumi," contributes to "La Parfumerie Moderne," October, 1920, an interesting account of his re-

\*From *The Chemist and Druggist*, Oct. 30, 1920.

cent visit to Vigone and Pancalieri, the centers of the cultivation, and also of the distillation of peppermint in the province of Turin. This district, which the author designates as the "Mitcham of Italy," yields annually about eleven million kilograms of peppermint, from which 25,000 to 27,000 kilograms of essential oil are obtained. The extensive cultivation of peppermint in Piedmont is of recent date, and is due to the action of a French distiller, M. Honoré Carles, who, observing that the locally-grown peppermint gave a very poor yield of essential oil, had ten bags of Mitcham-quality plants sent from England, which he distributed in 1900 to the growers of Pancalieri. The plants thrive remarkably well, and may now be regarded as a special variety, indigenous to that district. The oil distilled from these plants, and sold under the designation of "Piedmontese Peppermint Oil," or, better, as "Italo-Mitcham Peppermint," is now acknowledged to be one of the best in the world, on account of the delicacy of its perfume and the sweetness of its aroma. This variety of peppermint yields about 1 kilogram of essential oil for every 400 kilograms of plants submitted to distillation. This year witnessed a normal harvest, but the price paid for peppermint was excessive. Whereas distillers had been prepared to pay 24 to 25 lire per 100 kilograms, the growers raised the price to 30 lire. This unexpected advance in price is due to the fact that the distillers work independently of each other, each trying to obtain from the growers the largest possible quantities of mint, promising them higher prices. Thus the growers succeeded this year in making a profit of 100 per cent. by taking full advantage of the competition among the distillers. A suggestion of the author to form a syndicate received a very unfavorable reception from the distillers, in view of the conflicting interests among the latter.

All the oil distilleries visited by the writer worked continuously, day and night, for a period of twenty-five days. The most important are: R. Subinaghi & Co., which possesses eight distilling plants, with a capacity of 400 kilograms each; Barbero-Rosso & Co., with two large plants of 650 kilograms each, and six of 350 kilograms, both of which are at Vigone. At Pancalieri there is the factory, already alluded to above, of H. Carles, with twelve distilling plants, of a capacity of 250 kilograms each; he also possesses another distillery, with four average-size plants, at Polonghera. The distillery of Sig. G. Varino, now managed by his son, is the oldest one producing peppermint oil in Italy; Sig. Varino, who died this year,

created this branch of industry in 1871. His factory has seven distilling plants of 400 kilograms each, in addition to two other factories, at Lombriasco, with five, and another at Polonhera, with four distilling plants. There are also a number of other distilleries, of minor importance, scattered throughout this district, such as Galasso Andrea, Rittatore, Barberi & Co., Ubertino Vignolo, etc. In conclusion, Sig. Micheletti insists upon the necessity for the Italian Government to promote more actively this branch of national industry, and points to the recent French Lavender Congress (*C. & D.*, Sept. 11, 1920, p. 68), as an example in point.

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#### IPECACUANHIC ACID.\*

An exhaustive study of ipecacuanhic acid has been made by R. Huerre (*Jour. Pharm. Chim.*, June 1, 1920), which affords a valuable contribution to our knowledge of this substance. In view of the extensive use made of emetine in the treatment of amoebic dysentery, it is interesting to note that the author attributes the curative value of de-emetinized ipecacuanha solely to its content of ipecacuanhic acid. The presence of this acid in ipecacuanha was already recognized in the French Codex of 1818, when Pelletier believed it to be gallic acid. It was first isolated by Wiilgk, in 1850, by means of lead subacetate; Wehmer, in 1911, described it as a glucoside, a view shared by Kobert. The method adopted by Huerre for isolating ipecacuanhic acid consists in exhausting the powdered drug with twenty times its weight of boiling distilled water, in four successive extractions. The collected liquids are filtered and evaporated to double the weight of the drug employed. This residue is again filtered and an excess of ammonium sulphate added. The precipitate is separated by filtration and washed with a saturated aqueous solution of ammonium sulphate, and then treated with alcohol (90 per cent.). The alcoholic extract is submitted to distillation, and when all the alcohol has been removed on cooling, the ipecacuanhic acid separates out from the residue, which consists of a

\* From *The Chemist and Druggist*, Oct. 9, 1920.

saturated aqueous solution of ammonium sulphate. It is then brought into solution by the addition of alcohol, after removing the water, filtered, and the alcoholic filtrate is evaporated to dryness. The product thus obtained still contains traces of ammonium sulphate, which can be removed by means of neutral lead acetate, which does not precipitate the ipecacuanhic acid, and then using lead subacetate and sulphuretted hydrogen. It occurs as a reddish, amorphous, very hygroscopic powder, with a bitter taste, soluble in water, alcohol, and ether. With ferric chloride it yields a green coloration, which changes into violet on the addition of ammonia. The author found that ipecacuanha root contains from 3 to 4 per cent. of ipecacuanhic acid, and further that the various official alcoholic preparations of this drug contain the total amount of acid present in the drug.

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#### THE DISTRIBUTION OF ACETONE IN THE BODY.\*

In certain conditions, both physiologic and pathologic, acetone may be present in the organism in amounts not negligible. At times it becomes a matter of considerable importance to obtain dependable information about them. While it is circulating in the blood stream, acetone may appear in the urine and expired air. The view that the acetone substance—acetone, aceto-acetic acid and beta-oxybutyric acid—are derived in large part from improper and incomplete metabolism of fats in the body has been generally accepted. The importance of careful observations of ketosis, as well as the abnormalities of carbohydrate transformation in the organism of the diabetic, is daily being better appreciated by discriminating clinicians, so that perversions in the metabolism of fat are receiving far more attention than in the past. There is no more potent agency in the prevention of ketosis and the acidosis related to it than the withdrawal of fat from the diet, wherefore Joslin<sup>1</sup>

\*From *Jour. Amer. Med. Assoc.*, Nov. 6, 1920.

<sup>1</sup> Joslin, E. P.: "Treatment of Diabetes Mellitus," Philadelphia, 1917, p.

has trenchantly remarked that fat at one time may save the life of the diabetic, but at another may destroy it.

Widmark<sup>2</sup> has recently demonstrated at the physiologic institute in Lund, Sweden, that free acetone belongs to the group of substances that can with the greatest ease penetrate living cells. Hence they diffuse readily throughout the organism and tend to avoid undue concentration at any locality or in any special tissue. Acetone itself passes into the urine by the process of diffusion; hence the concentration of this compound in the blood and urine is usually the same. Aceto-acetic acid (diacetic acid), to which the well-known ferric chloride urinary test of Gerhard is attributable, depends on the characteristic secretory functions of the kidneys for its elimination; consequently its concentration is commonly higher in the urine than in the blood.

It also appears from the observations of Widmark<sup>3</sup> that the elimination of acetone through the lungs is a pure diffusion process. From his data there is no reason to suppose that any secretion of the volatile compound takes place, such as has at times been assumed for the passage of certain gases through the alveolar membranes. From a simple determination of the concentration of acetone in the alveolar air, so commonly collected nowadays in the estimation of carbon dioxide factors, it is possible to secure an accurate calculation of the free acetone concentration of the blood. Widmark points out that accordingly in a diabetic, by combined blood estimation and analysis of alveolar air, one may arrive at an understanding of the relationship between the free acetone and the total acetone in the blood. The method, he adds, has this great advantage, that the relationship between the acetone and the aceto-acetic acid can in no way be disturbed by the analysis; the separation of the free acetone from the aceto-acetic acid is effected, so to speak, with the organism itself as distillation apparatus. The ability to differentiate and estimate the various ketone substances with accuracy, as is already accomplished for the sugar in the blood and urine of glycosuric patients, is likely to prove helpful in the clinic of diabetes.

<sup>2</sup> Widmark, E. M. P.: "Studies in the Acetone Concentration in Blood, Urine and Alveolar Air. II. The Passage of Acetone and Aceto-Acetic Acid into the Urine," *Biochem. J.*, 14: 364 (July) 1920.

<sup>3</sup> Widmark, E. M. P. *Ibid.*, p. 379.

## CURRENT LITERATURE

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### MEDICAL AND PHARMACEUTICAL NOTES.

FATAL CASE OF AMYLENE HYDRATE POISONING.—Jacobi and Speer report what, as far as they know, is the only case of fatal tertiary amyl alcohol poisoning on record. Six grams of amylene hydrate as an enema had been prescribed for an epileptic, age 22, as he was having series of seizures that did not respond to bromides or other remedies. Twenty-two hours later, it was discovered that through a mistake of the nurse the patient had been given 35 c. c. in place of 6 gm. The twenty-fourth hour edema of the lung and cardiac insufficiency were present. After the forty-second hour, gastric hemorrhage occurred (about one litre of a black, coffee-ground-like substance). Shortly afterward the reflexes returned, beginning with the plantar reflex. The intoxication seemed to be overcome, but seven hours later death occurred, accompanied by a rise of temperature. Ancker reported in 1892 a woman's attempt at suicide by taking 27 gm. of amylene hydrate, approximately the same amount that this patient received. The woman recovered, and the writers think that their patient would in all probability have recovered from the intoxication if it had not been for the severe complication of influenzal pneumonia. (From *Therapeutische Halbmonatshefte*, Berlin, through *Jour. Amer. Med. Assoc.*, December 4, 1920.)

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ACTION OF SODIUM OLEATE ON GONOCOCCUS.—Sodium oleate was found by Davis and Swartz to have a definite germicidal value for the gonococcus. This value is increased, where uncoagulated protein is present, by the addition of 0.5 boric acid. The presence of small sublethal quantities of sodium oleate, 1:8,000, increases the germicidal action of many drugs against the gonococcus. With others it is without effect. Sodium oleate with boric acid is suggested as an adjuvant to other drugs in the treatment and prophylaxis of gonorrhea. (From *Jour. of Urology*, Baltimore, through *Jour. Amer. Med. Assoc.*, December 11, 1920.)



EUCALYPTUS LEAVES FOR DIABETES.—As the result of a paper published in the *Revue horticole d'Alger*, the treatment of diabetes by infusion of eucalyptus leaves has been frequently tried. Dr. Perez, in a communication to the author, says that after reading of the good effect produced by the drug many experiments had been made, and complete success attained; he did not think there were any more cases of diabetes in the island (Teneriffe). A very marked aphrodisiac action was also observed. Dr. Trabut has himself frequently prescribed it with very favorable results. A decoction of 10 to 15 gm. of leaves in 500 c. c. of water is employed, but a liquid extract would probably be a more convenient preparation. (*Bull. Gen. de Therap.*, 171: 428; through *The Pharm. Jour. & Pharmacist*, September 18, 1920.)

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FATAL POISONING WITH METHYL BROMIDE.—Goldschmid and Kuhn relate that after a kettle containing 178 kg. of methyl bromide had exploded, the men resumed work in the room, noticing merely a transient aromatic odor. There were absolutely no symptoms at first, but the second day afterward two or three of the men complained of dizziness or unstable balance, and the room was evacuated for twelve days. Then work was resumed and the men left that evening in apparent health, but one was found dying on the street, and two others presented similar symptoms in a day or two; with only a brief prodrome, epileptiform convulsions developed suddenly, with loss of consciousness and pulmonary edema, fatal in a few hours. Six others were treated in the hospital for dizziness, headache, loss of balance and general depression, but there was no disturbance in vision, no nausea, no vomiting, and the blood findings were normal. The men regained their earning capacity, but still showed, eight months later, occasional tremor of the hands and tongue, and the Romberg sign was weakly positive. The clinical picture thus differed from that of the few cases of methyl bromide poisoning on record. Necropsy revealed acute changes in the ganglion cells of the cortex in each fatal case. Pulmonary edema and suppurative bronchitis were found also in the one case examined. (From *Zentralblatt für Gewerbehygiene, etc.*, Berlin, Feb., 1920; 8, No. 2, through *Jour. Amer. Med. Assoc.*, Oct. 16, 1920.)

INDICAN IN SERUM AS TEST OF KIDNEY FUNCTIONING.—The indican content and urea content of the blood serum of forty patients with different diseases are tabulated to show the variations with dieting and other factors, and the importance of hyperindicanemia for the prognosis. With the simple test described, it is possible in every case of uremia to obtain deeper insight into conditions and foresee the outcome. Haas accepts 1.4 mg. per liter as the limit of the normal range; Rosenberg's limit is from 1.5 to 1.8 mg. The urea and the indican content do not run parallel, although when there is uremia there is usually indicanemia, and in one case hyperindicanemia was found before the uremia developed. In one case of contracted kidney the urea was at first 1.17 per thousand, the indican, 1.7 mg. per liter, the figures on repeating the tests were 1.06 and 1.08 urea and 6.4 and 21.3 mg. indican. This patient had been kept on a protein-poor diet. In another similar case the urea figures were 1.46, 1.04 and 0.52 per thousand on repeated tests, while the indican figure kept persistently at 4.27 mg., thus testifying that the condition was grave, although the urea content was normal. Both of these patients died within a short time with uremic symptoms. The protein-poor diet reduced the uremia but did not modify the hyperindicanemia, and the latter was thus the true basis for prognosis. (From *Nederlandsch Tijdschrift v. Geneeskunde*, Amsterdam; through *Jour. Amer. Med. Assoc.*, October 23, 1920.)

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BENZYL BENZOATE IN HYPERTENSION.—Benzyl benzoate has been shown to be a powerful vasodilator, without being depressant to the heart when administered by mouth in small doses. Owing to this property Macht found it to be effective in the treatment of hypertension and angina pectoris. The best method of administering the drug in such cases is in alcoholic solution, which admits of rapid absorption and control of the dose. A 20 per cent. alcoholic solution of benzyl benzoate was administered by mouth, either in cold water or milk. The ordinary dose was found to be 20 or 30 drops of such a solution, taken three or four times a day. After administering to a patient full doses of benzyl benzoate and obtaining a desirable therapeutic effect, the reduced pressure could be maintained by keeping a patient on very small doses of the drug, sometimes no more than 5 minims of the 20 per cent. solution. The effect of benzyl benzoate on the blood pressure was demonstrable

even in such cases in which nitrites failed to produce a vasodilation. (From *New York Medical Journal*, Aug. 28, 1920, through *Jour. Amer. Med. Assoc.*, Sept. 11, 1920.)

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TREATMENT OF ITCH BY ALCOHOLIC SOLUTION OF BETANAPHTHOL.—If alcohol is used as the vehicle for applying betanaphthol as a parasitocidal agent, it enables the latter to come into close contact with its intended object. The solution penetrates into the folds of the skin, into the tracks of the sarcoptes, into the spaces and into the intercellular interstices of the epidermis. It dissolves the fats in the capillary spaces and is absorbed into these. The solution kills the parasite, and prevents further infection of all kinds. The alcohol should be 94% or more. For an adult the proportion of betanaphthol for use should be 7 to 10%, according to the state of the skin; and this can always be diluted to 5% for patients with deep lesions, produced by scratching, in whom the stronger solution would cause pain. The itching usually disappears after the first application, because betanaphthol has an anæsthetic effect, and this may be increased by the addition of 1% of menthol. The skin should be dry, and the lotion applied by means of a swab, moistened in it; this is passed carefully over the whole surface of the skin without rubbing. The application is made twice daily for two or three days. (From *The Pharm. Jour. and Pharmacist*, Sept. 4, 1920.)

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## CORRESPONDENCE

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### PROGRESS OF THE PHARMACOPŒIAL REVISION.

Philadelphia, January 1, 1921.

TO THE EDITOR:

A summary of the activities of the Committee of Revision of the United States Pharmacopœia, tenth revision, covering the first six months, accompanies this note.

It is a definite policy of the Committee of Revision to make public its decisions and invite comment. As the revision progresses, all important decisions will be announced and the members of the

committee will welcome comments from any one who is interested in the revision.

It is difficult for those who are not closely affiliated with the work to appreciate the enormous mass of detail which must be considered, but I am happy to say that from my experience in previous revisions I am confident that the work is progressing satisfactorily and with a notable speed and earnest determination on the part of the members to bring it to the earliest possible conclusion.

Very truly yours,

..

E. FULLERTON COOK,  
*Chairman.*

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## PROGRESS OF THE PHARMACOPŒIAL REVISION.

About six months having passed since the Pharmacopœial Convention in Washington and the election of the Committee of Revision, a brief outline of the work of the committee during this period is presented, carrying out the idea of publicity, which is a well-defined policy of the work of revision.

The personnel of the Revision Committee was fully reported at the time of the convention and also the fact that in the personal conferences which immediately followed the election of the committee, an organization was perfected which permitted the immediate start of the revision.

The sub-committees, with their chairmen, differ slightly from those of the last revision, two new sub-committees being created and other sub-committees being consolidated.

The sub-committee on Bio-Assays and on Reagents and Test Solutions, formerly taken care of as the work of other sub-committees, were considered important enough to be established as new divisions of the work.

The appointment of the sub-committees, their organization and election of chairmen and the appointment of these chairmen as the members of the Executive Committee during the Washington conferences, were subsequently approved by the vote of the Committee of Revision and the Board of Trustees, as required by the by-laws of the convention.

The Executive Committee and sub-committees are as follows:

Chairmen of Sub-Committees and Members of the Executive Committee.	Sub-Committees.	Number of Each.
E. Fullerton Cook, Ph. M., Chairman of the Executive Committee.		
1. H. C. Wood, Jr., M. D.	No. 1— <i>Scope</i> (Admissions and Dele- tions). Barbour, Bastedo, Beringer, Christ'an, Craig, DuMez, Edmunds, Fantus, Fussell, Hamburger, Hatcher, Hodge, Hunt, LaWall, Leonard, Rowntree, Seltzer, Sollmann, Stitt, Wood, Zeigler.	21
2. Torald Sollmann, M. D.	No. 2— <i>Therapeutics and Pharmacody- namics</i> (Posology). Bastedo, Fussell, Sollmann, Wood.	4
3. C. W. Edmunds, M. D.	No. 3— <i>Bio-Assays</i> . Anderson, Barbour, Edmunds, Hatcher, Houghton, Hunt, McCoy, Pittenger, Zeigler.	9
4. George W. McCoy, M. D.	No. 4— <i>Bio-Products and Diagnostical Tests</i> . Anderson, Edmunds, Houghton, McCoy, Pittenger, Stitt.	6
5. Henry Kraemer, Ph. D.	No. 5— <i>Botany and Pharmacognosy</i> . Alsberg, Dye, Gathercoal, Kraemer, Newcomb, Richtmann, Schneider.	7
6. Charles E. Caspari, Ph. D.	No. 6— <i>Proximate Assays</i> . Caspari, Dohme, Eldred, Havenhill, Johnson, Ruddiman, Scoville.	7
7. H. V. Army, Ph. D.	No. 7— <i>Inorganic Chemicals</i> . Alsberg, Army, Bradley, Caspari, Clark, Eldred, Havenhill, Jordan, LaWall, Murray, Rosengarten.	11
8. George D. Rosengarten, Ph. D.	No. 8— <i>Organic Chemicals</i> . Army, Caspari, Clark, Dohme, Johnson, Jordan, Murray, Rosengarten.	8
9. C. H. LaWall, Ph. M.	No. 9— <i>Reagents and Test Solutions</i> . Army, Bradley, Clark, Eldred, LaWall, Murray, Nitardy, Rosengarten.	8
10. W. O. Richtmann, B. S.	No. 10— <i>Volatile Oils</i> . Alsberg, Dohme, Gathercoal, Johnson, Richtmann.	5

Chairmen of Sub-Committees and Members of the Executive Committee.	Sub-Committees.	Number of Each.
11. G. M. Beringer, Ph. M.	No. 11— <i>Extracts, Fluidextracts, Tinctures.</i> Beringer, Francis, Havenhill, Kelly, Nitardy, Ruddiman.	6
12. Wilbur L. Scoville	No. 12 — <i>Waters, Solutions, Spirits, Syrups, Elixirs.</i> Beringer, Culley, Dye, Fantus, Kelly, Ruddiman, Scoville, Seltzer.	8
13. Jacob Diner, M. D.	No. 13— <i>Cerates, Ointments and Miscellaneous Galenicals.</i> Culley, Diner, Dye, Francis, Kelly, Seltzer.	6
14. Theodore J. Bradley, A. M.	No. 14— <i>Tables, Weights and Measures.</i> Bradley, Caspari, Diner, DuMez, Jordan.	5
15. A. G. DuMez, Ph. D.	No. 15— <i>Nomenclature.</i> Craig, DuMez, Kraemer, Newcomb, Fantus, Schneider, Stitt, Wood.	8

Another feature of the Washington conference was the consideration by the Sub-committee on Scope of the articles official in the U. S. P. IX. It was understood that all those articles for which there was no negative vote cast for admission to the U. S. P. X. would be reported at once for inclusion in the new Pharmacopœia. Material was thus provided for immediate revision. The Sub-committee on Scope within a short time reported about five hundred titles for admission and these articles have been before the various sub-committees for some months.

*Scope.* A significant action taken at the Washington conference related to the policy to be followed by the Committee of Revision concerning admissions. There were many of those on the committee who believed that the final decision on admissions, so far as therapeutically useful substances were concerned, should be left to the medical members of the committee. Others believed that this decision should be subject to the majority vote of the entire committee and the matter was thoroughly discussed and the following motions finally approved:

"In questions concerning the inclusion of substances of therapeutic usefulness in the Pharmacopœia, the entire body of physicians on the Committee of Revision shall have the deciding vote."

"In all questions regarding the inclusion of substances of pharmaceutical necessity, the entire body of pharmacists on the Committee of Revision have the deciding vote."

When the Washington conference had adjourned several members requested that this action on Scope be reconsidered by mail and an opportunity was again given to every member of the committee to present arguments. These were published in full in the committee circulars and a new vote taken. Again the motions were approved by the committee. The practical operation of this decision resulted in immediately placing before the committee the decisions of the Sub-committee on Scope. This consists of a list of those substances now in the U. S. P. IX., which are approved for admission and also the names of such new articles as may be deemed worthy of recognition. Members of the Committee of Revision are invited to comment upon the reports on Scope, and if there is a question raised concerning the decisions of the sub-committee, the articles under discussion will be reconsidered by all of the physicians of the Revision Committee, their vote is to be accepted as final. It should be explained that the Sub-committee on Scope consists of the seventeen representatives nominated by the medical members of the convention and also includes three pharmacists. There are at least six additional physicians on the Revision Committee and these will have a vote on all substances which must be reconsidered.

The reports of the Sub-committee on Scope will also be published in journals at a suitable time, that physicians and pharmacists may have an opportunity to express their opinion concerning the reported admissions or deletions and all of these comments will be placed before the committee before the final vote.

The motions, as will be observed, provide for the original decisions on therapeutically useful substances through the vote of the Sub-committee on Scope, with the final decision, if the original report is questioned, left to the vote of the physicians of the entire committee. In the same manner the inclusion of those substances of pharmaceutical necessity are left to the pharmaceutical members of the committee for final decision.

At the personal conferences the Revision Committee also adopted rules of procedure for the conduct of business in the committee, following very closely the rules in force during the last decade.

Considerable criticism had been received concerning the use of "mils" in the Pharmacopœia, and as the term had not been

adopted among chemists and the Bureau of Standards had recommended the use of the abbreviation "cc" as the standard abbreviation for cubic centimeters, the committee has voted to use "cc" in the new Pharmacopœia. The French spelling of the word "gramme" was also criticised and the committee decided to adopt the American standard spelling "gram." The theoretical argument that it might be mistaken for "grain" in prescription writing was considered unworthy of serious consideration, as no physician writes the word "gram" on a prescription.

#### ORGANIZATION OF THE CHAIRMAN'S OFFICE.

Soon after the convention the chairman's office was organized in Philadelphia. The necessary supplies, consisting of stationery, envelopes, binders and general equipment, were provided, and in August, 1920, the Board of Trustees authorized a rental of an office for the work. Here are concentrated all phases of revision activity and in this office are being mimeographed and issued the "Circulars" of the General Committee, the "Letters" of the Executive Committee, and the "Bulletins" of practically all of the sub-committees. There have already been placed before the various committees over six hundred pages of circular material.

#### SUB-COMMITTEES.

Every sub-committee is organized and at work. First reports on texts have appeared in some of the sub-committees and others are about ready to send in their first revised texts.

#### SPECIAL SUB-COMMITTEES.

The convention authorized the establishment of two special sub-committees, one on drug markets and the other to study and establish standards for permissible quantities of gruffs and trailings, resulting from the grinding of drugs. These two special sub-committees have been made subsidiary committees to the Sub-committee on Botany and Pharmacognosy, and Dr. Carl L. Alsberg has accepted the chairmanship of the work on Drug Markets and Professor E. L. Newcomb, of the Special Committee on Gruffs and Tailings.



AUXILIARY WORKERS.

As the number of the members of the Committee of Revision is limited, it was not possible for all those interested in the revision to be elected to the committee, but their assistance and co-operation in the revision of the Pharmacopœia was considered of great importance. Therefore the committee voted to invite the co-operation of auxiliary members to the several sub-committees. This action having been approved by the Board of Trustees, a number of auxiliary members have been nominated by sub-committee chairmen and approved by the Revision Committee and Board of Trustees. These associate members will take part in sub-committee activities but without vote or honoraria. Those on the first list are given below, and others have since been nominated:

*Biological Products and Diagnostical Tests:*

Prof. Wm. H. Park,	New York City
Dr. James P. Leake,	Washington, D. C.
Dr. John N. Force,	Berkeley, Cal.

*Inorganic Chemicals:*

Dr. Lyman F. Kebler,	Washington, D. C.
Dr. Wm. G. Crockett,	Richmond, Va.
Prof. Jeannot Hostman,	New York City.
Dr. Hugo H. Schaefer,	New York City.
Dr. Gaston DuBois,	St. Louis, Mo.
Dr. Virgil Coblenz,	New York City.
Dr. S. P. Sadtler,	Philadelphia, Pa.
J. P. Snyder,	Norwich, N. Y.
Prof. Joseph L. Mayer,	New York City.
Dr. W. F. Hillebrand,	Washington, D. C.

*Organic Chemicals:*

Joseph Rosin,	Philadelphia, Pa.
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*Reagents and Test Solutions:*

W. D. Collins,	Washington, D. C.
Joseph W. Ehman,	Philadelphia, Pa.
Ralph R. Foran,	Philadelphia, Pa.

*Cerates, Ointments and Miscellaneous Galenicals:*

William A. Hall,	Detroit, Mich.
Dr. Gustave Horstman,	New York City.
Otto Canis,	New York City,
J. L. Lascoff,	New York City
Dr. Curt Wimmer,	New York City.
Dr. Wm. C. Anderson,	Brooklyn, N. Y.
Edwin C. Hutman,	Albany, N. Y.

*Nomenclature:*

E. J. Crane, Editor of *Chemical Abstracts*, Columbus, Ohio.  
 Dr. Arno Viehoveer, Bureau of Chemistry, Washington, D. C.  
 Oliver A. Farwell, of Parke, Davis Co., Detroit, Mich.

*Botany and Pharmacognosy:*

Chas. M. Sterling,	Lawrence, Kans.
Mr. Butters,	Minneapolis, Minn.
Anton Hogstad, Jr.	Brookings, S. D.
Philip F. Fackensthal,	Richmond, Va.

*Gruffs and Tailings (sub-group under Botany and Pharmacognosy):*

E. L. Newcomb (Chairman),	Minneapolis, Minn.
C. L. Alsberg,	Washington, D. C.
George E. Ewe,	Philadelphia, Pa.
John Moser,	Baltimore, Md.
G. A. N. King,	Minneapolis, Minn.
Henry Kraemer ( <i>ex-officio</i> ),	Mt. Clemens, Mich.

## COMMENTS AND SUGGESTIONS.

All of the comments or criticisms of the U. S. P. IX. which were available, either through the Digest of Comments of the Public Health Service, or as submitted to the convention or to the committee within recent months, have been tabulated and placed before the Committee of Revision and the sub-committee chairmen. A letter has recently been sent to many of those interested in the Pharmacopœia, either as manufacturers of pharmaceuticals or chemicals or dealers in pharmacopœial products, again inviting suggestions, and any one who is in position to offer an improve-

ment for any pharmacopœial drug, chemical or preparation, or for other requirements of the Pharmacopœia, is invited to send this at once to the chairman, who will see that it is properly considered.

#### PUBLICITY.

From time to time important decisions of the committee and a report of the progress of the revision will be made public through the chairman's office, so that all may follow the work of revision. When revised texts have followed their regular course of sub-committee consideration, Executive Committee study, and are finally before the General Committee, an abstract of the proposed changes will also be published, giving every one who is interested an opportunity to know the new standards before they are actually printed. This plan was found of much value in the last revision and is fully in keeping with the policy of the present Committee of Revision.

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## BOOK REVIEWS

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"DICTIONARY OF EXPLOSIVES," By ARTHUR MARSHALL. XIV, 159 pages. P. Blakiston's Son & Co., Philadelphia, Pa., 1920.

The appearance of this little book is timely, as it has been twenty-five years since the publication of the last book of this kind—that by Cundill and Thomson, and during this time, especially during the past few years, there has been great activity in the development of commercial and military explosives. In his little "Dictionary" Mr. Marshall has given in concise form such information as is usually contained in Government bulletins on the various types of explosives having special or trade names. In individual cases the following facts have been given: Use, manufacturer, date of permit (or whether permissible), composition, limit, charge and power (as indicated by the ballistic pendulum). In the case of some of the British explosives this information is fairly complete, but in the case of American, German, French and other explosives the information is usually meager.

Preceding the dictionary proper there is a classification of explosives into the following groups:

Coal mine explosives, blasting explosives, high explosives, mis-

cellaneous explosives and propellants. The first group, coal mine explosives, is sub-divided according to the country producing them. The numbers listed under the names of the different countries give a good idea of the prominence which the author naturally extends to British explosives throughout the book. These numbers follows: American, 32; Austrian and Hungarian, 4; Belgian, 22; French, 5; German 47 and British 99. In the list of propellants only four out of the sixty-six mentioned are of American make.

Following the dictionary proper there is an "index" of explosive ingredients which lists under the name of each ingredient, the names of the explosives, in this book, containing it. This index is of value in showing the extent of the use of each ingredient.

In spite of its incompleteness as regards American and German explosives, Marshall's Dictionary will be of considerable interest and value to manufacturers of and dealers in explosives, as it includes many of the new explosives which have proved a commercial success.

CHARLES E. VANDERKLEED.

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"LABORATORY EXPERIMENTS IN ORGANIC CHEMISTRY." By E. P. COOK, A. M., Associate Professor in Smith College. 2d Ed., 79 pages, 8 illustrations. \$1.00 net. P. Blakiston's Son & Company Philadelphia, Pa.

This book is designed especially for use with Stoddard's "Introduction to Organic Chemistry. The experiments are those proven most suitable for a first course in organic chemistry and illustrate and emphasize the more important class reactions, both as to the manufacture and testing of members of the several classes of organic compounds.

Only experiments that will "work" are claimed to be given. Equations have been omitted, it being considered best to allow the student to work them out for himself with the aid of his text-book. Reference is made to seven other books for details of some operations. The procedure outlined for the conduct of the experiments is concise and generally easily followed. Interspersed with the explanations are numerous questions designed to draw from the student what he is doing and seeing, and thus impress indelibly on his mind the salient facts and significance of his work.

F. P. STROUP.

TRAVAUX DU LABORATOIRE DE MATIÈRE MÉDICALE DE L'ÉCOLE  
SUPÉRIEURE DE PHARMACIE DE PARIS, Vol. XI, 1917-1919.  
Publishers, Vigot Frères, Paris.

The volume before us contains a series of theses contributed as researches from the Materia Medica Laboratory of the School of Pharmacy of the University of Paris. These are arranged in five parts:

The first is a study of the histological characteristics of the natural woods of Madagascar and a comparison of these with the principal woods used in the industries in Europe. This thesis has been prepared by André Gérard. In the consideration of each specimen the history, macroscopic characteristics, the microscopic examination of sections, the physical properties and the technical uses are carefully described. The botany of the wood and the source from which each authentic sample examined by the student was obtained, the synonyms and vernacular names employed in the country from which obtained, the habitat and bibliographical references are given with each description. The cellular structure, as shown by sections of the wood and bark, is well described and the illustrations furnished in each case demonstrate these characteristics nicely. The cellular contents and the physical and chemical properties are also generally stated.

This monograph of about 160 pages is ended with tables setting forth the chemical properties of these woods, their indigenous names and botanical classifications.

The second part of the book is a thesis on the Alkaloidal Content of Cultivated Belladonna, submitted to the University of Paris by Frederic Beausite for the diploma of Doctor in Pharmacy.

The author carefully reviews the literature and methods for the preparation of the extract of belladonna, the various methods for its assay, the effect of soil constituents, climatic conditions and the time of cultivation. These questions are exhaustively considered in this thesis.

The third part is devoted to a thesis on the Java Coca, being a monograph on the history, botany, chemistry and pharmacology, by Mlle. Emma Reens, likewise submitted to the University of Paris for the diploma of Doctor in Pharmacy. It appears that *Erythroxylon Coca* has become an important article of cultivation and commerce in Java and likewise in Ceylon. Statistical data as

to the amounts exported of both the leaf and alkaloid are given in tables. A careful review of the chemistry of the alkaloids of coca leaves with special consideration of that cultivated in Java is given in Chapter 3 of this dissertation. The other constituents of the leaves such as tannin and essential oil are described.

Chapter 4 is devoted to the methods of extraction of the alkaloids and Chapter 5 is devoted to the galenical preparations of coca and a comparative examination of these. In these the preparations official in the various pharmacopœias are given.

Chapter 6 considers the rational preparations of extracts of coca, and Chapter 7 the solutions of cocaine hydrochloride and their sterilization.

The author considers that the coca cultivated in Java is the *Erythroxylon Coca* var. *Spruceanum*, while that of Ceylon is principally Huanuco and both these are varieties of *Erythroxylon Coca* Lamarck.

The anatomical structure of the Java leaf is described and cross sections, the upper and lower surfaces are illustrated.

The fourth part of this book is a thesis on the methods of micro-chemical research upon certain constituents of essential oils, submitted for the "Doctor" degree by René Baudry. Numerous plates show the various types of crystals obtained in his investigations and excellently illustrate this study. The author has given considerable attention to determining the localization of essential oils in aromatic plants by the aid of reagents. This examination covers a variety of plants and parts thereof, such as leaves, flowers, seeds and denotes specially the characteristic micro-chemical reactions obtained with the anthranilate and the methylantranilate of methyl.

A bibliographical index concludes this thesis.

The fifth part, concluding the publication, is composed of a series of abstracts covering a variety of subjects, including stick-lac, preparation of cat-gut ligatures, lixiviation, preparation of potassium and sodium soaps, the utilization of the oleoaginous residues from the seeds of Meliaceae and the preparation and uses of surgical soaps.

The work throughout exhibits a high class of research in pharmacy.

G. M. B.

# THE AMERICAN JOURNAL OF PHARMACY

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## EDITORIAL

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### OUR HERITAGE.

The centennial observance of the founding of The Philadelphia College of Apothecaries, the initial movement in America looking toward the education of pharmacists, calls not only for retrospection, but likewise for earnest reflection. No man may know what the future has in store, or what the future may bring forth as the fruits of the labor of his day. It is, however, possible for each generation to build upon a foundation of good example that may prove an inspiration to others, and an incentive to a higher development of the vocations in which their labors are directed.

As we study the events and the work of the principal characters associated with this important occurrence in the history of pharmacy, we are impressed with the unselfishness of their labors, and the high ideals and motives that prompted and directed their course, and we are inspired with respect and reverence to their memories. It is evident the philosophy of service is not an exclusive doctrine of the present generation.

The history of The Philadelphia College of Pharmacy is one of continuous striving to uphold and upbuild the ethics of pharmacy, and the planting of new milestones along its course of progress. The founders planted better than they knew, and as a result of their labors and sacrifices and the continued service of those who followed in their foot steps, there is now dedicated not only a proper basic foundation but a superstructure that has been carefully erected as representative of ethical pharmacy.

Surely we have no mean heritage. Yet, with this heritage, we must appreciate that to the present generation there has come responsibilities. The torch of progress and of service now in our hands must be passed on to succeeding generations with augmented

knowledge, strength and brighter prospects. It is ours not only to preserve, but to deserve still greater results. We cannot live and work for self alone. The sacrifices and exemplary labors of our illustrious predecessors make it a compelling duty to sustain and carry on the work so well begun.

Upon the graduates of this old school, there is a special responsibility to maintain its prestige; to husband its strength; to support its ideals and labors, both by moral and material support. Who can estimate the value of the instructions that he has received within the walls of this old institution, or measure the effect thereof upon his professional and business career or to what extent his success in life is attributable to the sound principles regarding the commercial and professional dealings with his fellow men that were inculcated by these teachers? Thus each Alumnus must engage in conscientious reflection upon his own debt to his Alma Mater.

Not only have the Alumni of The Philadelphia College of Pharmacy cause to be thankful for the inauguration of The Philadelphia College of Pharmacy and its labors of the past one hundred years, but every branch of the drug trade, and every druggist throughout this broad land has benefited by its teachings and contributions to pharmacy. Its foundation was at a critical period when the action that was forestalled would have indefinitely subordinated the practice of pharmacy to that of medicine. Its influences have radiated far beyond its own class rooms. The scientific works that have emanated from its faculty, the knowledge that has been transmitted through its publications, its work in behalf of the U. S. Pharmacopœia and the National Formulary, and its interest in the improvement of the professional practice of pharmacy have spread over the entire globe.

The Philadelphia College of Pharmacy and Science is now completing its first one hundred years of continuous service in behalf of pharmacy. On the threshold of another century it is presenting well-defined and comprehensive plans for the future developments. It is apparent that the vision of the forefathers is to be duplicated by a still broader vision demanded by the commanding position and the conditions of the time under which it is entering upon its second century. With confidence its management asks for renewed pledges of support from Alumni and friends, so that these plans may be carried to consummation in keeping with the heritage that was ours.



## ORIGINAL PAPERS

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### THE CENTENARY OF PHARMACEUTICAL EDUCATION IN AMERICA.

By GEORGE M. BERINGER, A.M., Ph.M.

Upon the occasion of the one hundredth anniversary of an important event in the history of a nation or of an organization, it is appropriate that a more comprehensive retrospect be taken than that usual at the intervening annual commemorations. The founding of The Philadelphia College of Apothecaries on February 23, 1821, the first pharmaceutical society to be organized in the New World, had a broader significance than was foreseen at that time. The history of this College is of vital importance to pharmacy. As the pioneer in pharmaceutical education it has had an incalculable influence in deciding the ideals of the profession. It has been a potent factor in determining the systematic collegiate education of pharmacists, and the influence radiating from its halls have been exemplary and of untold benefit to the various branches of the drug trade, as well as to the strictly professional work of the pharmacy.

On the centennial of such an important pharmaceutical event, our thoughts naturally turn to a review of the political and social conditions existing at the time, both in America and in Europe; the acts and influences that led up to the establishment of a college for the tuition of pharmacists, and to those who were the active and guiding spirits in this movement.

Europe and America alike had but recently had a surfeit of war. The Napoleonic campaigns had affected the integrity of the European countries, and the Holy Alliance had but recently been formed to support the second treaty of Paris and to secure permanent peace in Europe. To the South, the Spanish Colonies were fighting their mother country for independence, and the Central American and the South American Governments were being established.

The Anglo-American War of 1812-15 more firmly established our own Federal Government and clearly defined the attitude of

the United States against all foreign aggression. What was even more apparent at this time was the spirit of our people; the determination that we were to become one of the foremost peoples of the world; that the abundant natural resources and the fertility of our soil should be applied to the end of developing our industries and national strength. Soon after the close of this war, and as a logical sequence thereof, arose the cry for financial and industrial independence from England, and this was the period of the inception of what has been referred to as "The American Policy"—"The Protective Policy." The foremost advocate at the time was A. J. Dallas, a Democrat of prominence and a former Secretary of the Treasury.

Our country experienced the usual aftermath of war, speculation was rife, state banks were established everywhere and with the usual result the inordinate bubbles burst and brought on a panic. Eighteen hundred and nineteen is said to have been a hard year, and farms were sacrificed, factories were closed, and Philadelphia was crowded with men out of employment. At that time Philadelphia was the chief city in America, not only in numbers, but likewise in financial, commercial and educational facilities. This period of our national history has been termed as the Period of Great Beginnings. The national ambition was a powerful incentive for many of the schemes for the development of our country, and Philadelphia was the center from which many of these can be traced.

The chartering of the Bank of Pennsylvania in 1816, for twenty years with the financial backing of Stephen Girard and other active financiers of the day, was an influential factor in encouraging many of our industries and public utilities. The first two years of its existence, like its predecessor, the first Bank of the United States, this bank was domiciled in Carpenters' Hall. Canals, railroads, turnpikes and bridges were among the leading public projects inaugurated, and the importance of transportation to the development of our country was thus recognized and claimed prime consideration. One of the feats of transportation of these early days was the bringing of coal by "arks" down the Lehigh and Schuylkill Canal to Philadelphia.

Eighteen hundred and twenty marks also a renaissance in the sciences, literature and arts. The old theories, such as the phlogistic theory in chemistry, that had so long hampered scientific

progress, had about run their courses, and now more rational ideals prevailed that laid the foundation for the great advance of the succeeding century in physical, chemical and in natural sciences. This was the time of the extension of scientific pursuits and the organization of scientific societies in America. Likewise, was it the time when new industries were being organized in every direction, and our artisans were becoming more skilful and ingenious. Education was claiming its due share of attention and schools and colleges were being instituted in various sections of the country. The foundation for a distinctive American School of Literature was being laid.

The year 1821 commences a new era in the history of pharmacy. Samuel F. Troth, in 1864, gave the following word picture of the condition of the practice of pharmacy at this time and the dependence of the early drug trade upon foreign sources of supply.

"Epsom salts was very little used when I was an apprentice; we used to purchase from 20 to 40 pounds of Glauber at a time, at 2¼ cents per pound, while we would only buy a single keg of Epsom, holding about 25 pounds, at 15 cents. The first really nice Epsom salts I recollect having in our store, was the year the College was organized; John Farr, the noted chemist, was going to pay a visit to his friends in London, and offered to make some purchases for us, and one of the articles in that first importation of our house was two casks, 1190 pounds of beautiful Epsom salts, at a cost here of 7 cents per pound, which was so much in demand by the retailers that we increased our orders, until the Baltimore manufacturers put a stop to our importations of the article. Super, carb. soda, which has been such a common and universally used article of later years, was hardly ever seen when I was learning the business; I think the first we had in our store, was purchased from Farr & Kunzie at \$1.25 per pound, in 1821, when we paid them the same price for tartaric acid.

"I attended the first and second courses of lectures of this Institution, and should have applied for the diploma had there been any such prize to have been obtained, but the College did not even decide upon the form of a diploma until I had been in business for myself between three and four years.

"Forty years ago, all the calcined magnesia we sold was burned in Abram Miller's pottery, opposite this building, where the public school now stands; we used to take a case of English carb. magnesia, pick out some of the nicest and hardest lumps, and pack the balance in earthen crocks procured from the pottery, and send them around to be put in the kiln when Miller burned his ware."

During the Colonial period, the several branches of medicine were conducted in a rather primitive style. The population was

largely rural and scattered over a wide area in this sparsely settled country along the Atlantic seaboard. The prevailing good health of the early settlers, and the custom of each family to have its collection of medicinal herbs and household remedies, which were employed in the home treatment of the simpler ailments, made the services of the physician needed only in extreme illness, epidemic or accident. The physicians in this period were a rather heterogeneous lot, some practicing medicine only as a portion of their life vocation. Most of these had only served an apprenticeship with some older physician, and by preparing the medicines he dispensed, observing his methods and studying under his guidance had completed the time of their indenture, and his certificate of proficiency was the only license to practice required. Some few, with higher aspirations, pursued their medical studies further in the European schools of medicine for the purpose of obtaining a diploma. The number of these better qualified physicians were augmented from time to time by a few educated medical men who immigrated from abroad. A writer states: "In those days any one who knew jalap from ipecac or Calomel from Tartar Emetic, and had the assurance to use them at his option, to make and apply ointments and plasters, to dress wounds, to splint a broken limb, was a welcome settler and received without asking the title of doctor.

In this primitive condition of the medical practice, the art of the apothecary was not recognized, and the dispensing of medicine was vested in the physicians. With the development of the Colonies and the growth of their commerce, the establishment of chemist stores and apothecary shops became more general. Many of the apothecaries were recruited from those who had served as apprentices to the physicians. The industrial and educational progress that had been made by the first quarter of the Nineteenth Century resulted in a stricter specialization in the arts, trades and professions, and this was reflected to some extent in the practice of the drug trade. The time had fully arrived for divorcing the art and practice of pharmacy as a distinct branch of medicine. The evolution of medicine had progressed to the state where a sufficient number of physicians realized the necessity and advocated dissociation as the proper line of progress.

Every event is the direct outcome of some pre-conceived teach-

ing and the attempt of some influential person or body of men to affect action in accordance therewith. With the result in evidence, it is usually easy to trace back to the original source the doctrines and theories from which the event sprung.

The institution of The Philadelphia College of Apothecaries was not a spontaneous occurrence of the time but was foreshadowed by a series of arguments and teachings promulgated since 1765. In that year Dr. John Morgan, returning from Europe, where he had assiduously applied himself to the study of medicine in London, Edinburgh and Paris, joined with Dr. Wm. Shippen, Jr., in founding the first medical school, the Medical School of the College of Philadelphia.<sup>1</sup>

In his "Discourse Upon the Institution of Medical Schools in America," delivered at the commencement of the College of Philadelphia, May 30-31, 1765, he publicly advocated the introduction of the regular mode of practicing physic in Philadelphia.

As a graduate of the College of Physicians of Edinburgh, he had subscribed to its code of ethics adopted in 1754, which prohibited their fellows and licentiates "from taking upon themselves to use the employment of an apothecary, or to have and to keep an apothecary shop."<sup>2</sup>

Bringing back from Europe this advanced idea, Dr. John Morgan, as the first Professor of Theory and Practice of Physic in America, boldly championed the principle that medical men henceforth should confine themselves to prescribing, leaving to the apothecary the preparing and compounding of medicines. He consistently advocated the dissociation of surgery and pharmacy from the practice of medicine proper, and in this initial address argued:

<sup>1</sup> The medical department of the University of Pennsylvania was established in 1779, and in 1791 these two medical schools, by act of the Legislature, were united under the University of Pennsylvania.

<sup>2</sup> This action was an attempt to reform the practice of medicine as carried on in Great Britain in accordance with the law enacted in 1511, by which the right to practice medicine in England was vested in the "faculty of medicine," who were privileged to practice medicine, surgery and pharmacy. The apprentices and assistants of the medical practitioners were termed "Apothecaries." Their functions were the dressing of wounds, extracting of teeth, bleeding and preparing the medicines and compounding the prescriptions of their preceptors. In the American Colonies, this custom of the Eng-

lish practitioners had been followed and continued until the initiation of the dissociation movement advocated by Dr. Morgan.



DR. JOHN MORGAN

"We must regret that the very different employment of physician, surgeon and apothecary should be promiscuously followed by any one man. They certainly require very different talents.

"The business of pharmacy is essentially different from either, free from the cares of both, the apothecary is to prepare and compound medicines as the physician shall direct. Altogether engaged in this, by length of time he attains to that skill therein which he could never have arrived at were his attention distracted by a great variety of other subjects.

"The wisdom of ages approved by experience, the most certain test of knowledge, has taught us the necessity and utility of appointing different persons for

these different employments, and accordingly we find them prosecuted separately in every wise and polished country.

"The paying of a physician for attendance and the apothecary for his medicines apart, is certainly the most eligible mode of practice both to the patient and practitioner. The apothecary, then, who is not obliged to spend his time in visiting patients, can afford to make up medicines at a reasonable price, and it is as desirable as just in itself that patients should allow fees for attendance—whatever it may be thought to deserve.

"They ought to know what it is they really pay for their medicine and what for medical advice and attendance."

While in Europe he wrote, "I am now preparing for America, to see whether after fourteen years' devotion to medicine I can get my living without turning apothecary or practitioner of surgery." It is apparent that this erudite and accomplished medical leader of the time had a clear vision of the proper field to be occupied by the co-ordinate branches of medicine, and that the process of the evolution of medicine and the dissociation of these branches in America can be traced to his early teaching.

In the announcement of the opening of the first medical school appeared this succinct statement, "In order to render the course of

lectures the more extensively useful it is intended to introduce into them as much of the theory and practice of physic, of pharmacy and chemistry as can be consistently admitted." Dr. Morgan had served his apprenticeship with Dr. John Redman, and in this capacity doubtless he had been the apothecary apprentice of this popular physician, and subsequently he had served for thirteen months as apothecary at the Pennsylvania Hospital, so that he was qualified to instruct in this branch.

In 1789, Dr. Samuel P. Griffith was appointed Professor of *Materia Medica* and Pharmacy, and after the consolidation of the College of Philadelphia with the University of Pennsylvania in 1791, Dr. Griffith continued this same chair and under the same title. The teaching of pharmacy, as a distinct branch, however, was not considered. The University teaching was confined to that considered necessary to the practicing physician. There was, however, alive though dormant, the precepts instilled by Dr. Morgan as to the necessity for a special education for those who intended to follow the vocation of apothecaries. Dr. Joseph Carson, in the history of the Medical Department of the University of Pennsylvania states, "The course pursued by Dr. Morgan may be said to have given the original impulse to the cultivation of the profession of pharmacy and sanctioned its independent existence."

Possibly the condition of the drug trade at this time, and the lack of control over the quality of medicines, and the agitation that had been made over the appearance of a lot of spurious opium and other adulterated drugs on the market had much to do with awakening the public interest, and directing the attention of the University of Pennsylvania authorities to the apparent need for collegiate education of pharmacists.

At a meeting held on August 3, 1819, the trustees decided that the teaching of the pharmaceutical art should be a part of the duties of the Professor of *Materia Medica* and Pharmacy, and that a course of lectures should be established intended for pharmaceutical students. At a meeting held on February 6, 1821, as a further step, the trustees determined that the degree of "Master in Pharmacy" should be conferred upon pharmacists who had served an apprenticeship of at least three years with a respectable apothecary and passed an examination before the Professors of

Materia Medica, Chemistry and Pharmacy.<sup>3</sup> But, hereafter it shall be requisite for obtaining the degree that the candidates shall have attended at least two courses of lectures on chemistry, materia medica and pharmacy in the University.

The seed sown by Dr. John Morgan was now beginning to bear fruit, and pharmacy is very largely indebted for its position as an independent branch of the medical profession to the discerning wisdom of this earnest advocate for the pure practice of physic. It is to the credit of the medical faculty of the University of Pennsylvania that they recognized that the duties of the apothecary were distinct from those of the medical practitioner, and that pharmacists need a special collegiate education. The trustees were convinced that the time had now come for the inauguration of a systematic and scientific education for pharmacists.

That this action was both timely and wise cannot be questioned, nevertheless, this project of the University looking toward the establishment of a school for pharmacists aroused the latent energy and the dormant pride and self-respect of those most directly interested in the needs and requirements of the drug trade. The opposition became more pronounced as it was more thoroughly discussed. The conferring of this degree by the University upon sixteen of the apothecaries of the city but added fuel to the dissatisfaction and the advertisement of this degree by some of the recipients was to the disgust of their competitors. The pharmacists were compelled to realize that the time had come when a plan must be adopted for the systematic education of those who wished to follow the profession of pharmacy.

It is narrated that Peter K. Lehman, one of the old school of Philadelphia druggists, whose store was located on the south side of Market Street, below Tenth Street, went to Henry Troth, then engaged in the wholesale drug trade on Market Street, below Seventh, and giving vent to his sentiments, indignantly declared, "Henry, this won't do." This gave rise to the inquiry, "Why can't

<sup>3</sup> The minutes of the University of Pennsylvania disclose that the action of the University was the outcome of a letter from Professor John Redman Coxe, on March 7, 1820, suggesting the propriety of granting licenses, after examination, to apothecaries.



we have an institution of our own, train our own apprentices and ourselves supervise the qualifications of those seeking admission to our ranks?" It is told that they concluded that this was a feasible idea, and they proceeded to call on those engaged in the wholesale and in the retail drug trade and presented their suggestion.

The intensity of the opposition to the project of the University, and the favorable acceptance and of the new idea was quite evident. A meeting of the druggists and apothecaries of the City and Liberties of Philadelphia was called to meet at Carpenters' Hall, on February 23, 1821. At this meeting, Stephen North was called to the chair and Peter Williamson was appointed Secretary. The resolutions adopted by the Board



PETER K. LEHMAN

of Trustees of the University at their recent meeting had been printed in Poulson's *American Daily Advertiser*. These were read and resolutions offered by Henry Troth were adopted. These objected to the University instituting a school of pharmacy, and set forth that the method proposed by the trustees of that body was not suited to correcting the alleged abuses in the drug and apothecary business. A committee of nine was appointed to consider the subject and report on a proper mode of procedure at a subsequent meeting. This committee, remarkable for the personnel and the ability of its members, consisted of Samuel Jackson, Daniel B. Smith, Robert Milnor, Peter Williamson, Stephen North, Henry Troth, Samuel Biddle, Charles Allen and Frederick Brown.

The second meeting was held on March 13, 1821, and the minutes record that this committee made a report setting forth that abuses had occurred of deteriorated drugs being introduced into the shops; and valuable remedies in daily use being adulterated

and sold of inferior quality; such abuses, attributable in part to want of proper pharmacological information on the part of some druggists and apothecaries who vended and physicians who buy, had attracted the attention of those interested in the proper conduct of the trade, and had led to some druggists and apothecaries at the suggestion of one of the faculty of medicine of the University, to direct the attention of the trustees to the subject, in consequence of which they have taken the action reported at the previous meeting. It was, however, apparent that the measures proposed by the University were not well adapted to correct existing irregularities, which could be best remedied by the interposition and active agency of the druggists and apothecaries themselves.



CARPENTERS' HALL IN 1821

To this end, the foundation of The College of Apothecaries was recommended, the attention of which will be constantly directed to the qualities of articles brought into the drug market, in which subjects relating to their business and its objects can be discussed, and information beneficial and instructive to the trade communicated. It was recommended that a school of pharmacy

be erected, in which lectures designed especially for the instruction of druggists and apothecaries should be delivered.

A Constitution and By-laws had been prepared by the committee, and this was approved and signed.

The following sixty-eight names of representative druggists and apothecaries composed the list of charter members:

Charles Marshall,	Thomas Cave,
Stephen North,	Joseph Allen,
John Elliott,	Thomas Wiltberger,
William Lehman,	Isaac Thompson,
Charles Allen,	Matthias Pleis,
Jeremiah Morris,	George Babe,
Robert Milnor,	Jacob Bigonet,
Peter Lehman,	P. Thompson, Jr.,
Samuel Jackson,	William C. Poole,
Elisha Crowell,	Henry Troth,
James W. Simes,	Peter Williamson,
William Rovoudt,	Warder Morris,
Mordecai L. Gordon,	George H. Burgin,
William Heyl,	Frederick Klett,
John P. Wetherill,	Edward B. Garrigues,
Edmund Pryor,	Frederick Brown,
Thomas M'Clintock,	Caleb Ash, Jr.,
George D. Wetherill,	Wilson Jewell,
Thomas Oliver,	Charles Ellis,
William Baker,	Jeremiah Emlen,
Thomas A. Mason,	John I. Smith, Jr.,
Richard Jordan,	George Glentworth,
James L. Smith,	Edward Lowber,
Alexander Fullerton, Jr.,	Charles Thompson,
Algernon S. Roberts,	Charles Wetherill,
Solomon Temple,	Charles Yarnall,
Edward Needles,	Daniel Thatcher,
Daniel B. Smith,	Daniel Elliott,
Samuel Biddle,	Charles Treichel,
Eleazer Cohen,	Samuel P. Wetherill,
Charles Marshall, Jr.,	Thomas Evans,
James S. Ewing,	Henry M. Zollickoffer,
A. Eckey,	Charles Rizer,
Daniel Laws,	Anthony H. Morris.

Two weeks later the first stated meeting was held, and the following officers were elected:

President: Charles Marshall.

Vice-Presidents: William Lehman, Stephen North.

Treasurer: William Heyl.

Secretary: Daniel B. Smith.

#### BOARD OF TRUSTEES:

Samuel P. Wetherill,

Dr. Samuel Jackson,

Daniel Elliott,

Charles Allen,

Henry M. Zollickoffer,

Jeremiah Morris,

Henry Troth,

Peter Lehman,

Charles Marshall, Jr.,

Warder Morris,

Peter Williamson,

Daniel Thatcher,

Samuel Biddle,

Thomas M'Clintock,

Frederick Brown,

Thomas Wiltberger.

The history of pharmaceutical education and of pharmaceutical progress in the Western Hemisphere dates from these meetings held in Carpenters' Hall in February and March, 1821. Thus was established the first College of Pharmacy in America, the pioneer whose precepts and examples have been closely followed by many schools of pharmacy subsequently instituted.

Sacred are the memories associated with Carpenters' Hall. It holds second place only to Independence Hall as a place of meeting in which transpired events of the utmost importance in shaping the destiny of this nation. It was erected in 1770, by the Association of Master Carpenters of Philadelphia—"The Carpenters Company." Within its halls the first Continental Congress convened on September 5, 1774, and fifty-five men picked as representatives of the Colonies met and were thrilled by the eloquence of Patrick Henry, and guided in their deliberations and the framing of the Declaration of Rights, by such counsellors as Jefferson, Adams and Washington.

It is indeed a happy coincidence that pharmaceutical education in America had its birthplace in such a hallowed spot and, as pharmacists, in addition to our patriotic reverence for the historical building and its associations, we can with just pride look upon the meetings of the druggists and apothecaries in Philadelphia, one hundred years ago, as the declaration of rights of pharmacy and its professional independence.

As we look over the list of the founders and first officers of the College, we are impressed that it is an exceptional list of names and that many of these were men of more than usual ability and social standing who performed noteworthy services in their calling and likewise in public affairs. Our narrative of the occurrences associated with the institution of The Philadelphia College of Pharmacy would be incomplete without reference to the dominating spirits of these meetings.

Stephen North, who presided at the first meeting of the Apothecaries held in Carpenters' Hall, was second Vice-President of the College from 1821 to 1824, and first Vice-President from 1824 until the time of his decease in 1826. He was a worthy wholesale druggist, doing business at 14 North Second Street (old number), a few doors south of Christ's Church. Shortly before his death he removed to the northeast corner of Sixth and Market Streets.

Charles Marshall, the first President of the College, was the youngest son of Christopher Marshall, the "fighting Quaker," whose *Diary of the Revolution*, or "Remembrancer," is a Philadelphia classic, accepted as a valuable record of events of those stirring times and of the prominent participants. Christopher Marshall was born in Dublin, Ireland, November 6, 1709, and after emigrating to America, was for some years a resident of Bucks County, Pa., and a member of the Middletown monthly meeting. He first established himself in business in 1729, at Front and Chestnut Streets. In 1735, he purchased a property on the south side of Chestnut Street, above Second Street, where he opened an apothecary shop which was considered the most complete this side of New York City, and possibly the earliest of its type in the City of Philadelphia. Suspended over the projection of the gable roof on Chestnut Street was a large gilded ball, and the store was commonly known as the "Golden Ball."



CHARLES MARSHALL

In 1765, two of his sons, Christopher Marshall, Jr., and Charles

Marshall, were taken into partnership. In 1772, he withdrew from active participation in commercial matters, but, for years thereafter, continued to take an active interest in public affairs. Because of his militancy, he was expelled from membership in the Orthodox Society of Friends, and became one of the founders of the "Free Quakers." He was active in the movements in opposition to the aggressions of the Crown, and was a member of many of the Citizens' Committees appointed in connection with these movements. It is recorded in the *Congressional Record* that in 1776 Christopher Marshall of Philadelphia, the well-known druggist and much-respected member of the Society of Friends, was commissioned to look after the needs of the sick and wounded in the hospitals of Philadelphia.

Charles Marshall was born in 1744, and was well educated in the branches then taught, including Latin and Greek, and was possessed of a fine literary taste. He learned the drug business with his father, and was well qualified to conduct a drug store. He became the active manager of this business, his brother, Christopher Marshall, Jr., devoting a large portion of his attention to the shipping business, in which the brothers were associated in partnership with their older brother, Benjamin.

The enviable reputation of the Marshall Drug Store, established by the father greatly increased, and a laboratory for the boiling of oils and the manufacture of Ammonia Salts and other chemicals was established on North Third Street, near the stone bridge over the Cohocksink Creek. This firm supplied large quantities of medicines to the Colonial troops; those of Pennsylvania, New Jersey, Maryland, Delaware and Virginia obtained their medical supplies almost entirely from this store.

In 1801, Charles Marshall retired from active participation in the business. The firm continued, but did not confine its activities to the drug business alone, and in a few years became insolvent, by reason of loaning its endorsement, and involved all connected with it in bankruptcy. This was a sad blow to Charles Marshall, and on May 30, 1805, he addressed this letter to the Philadelphia monthly meeting, explaining his financial embarrassment:

"Altho my prospects be thus gloomy with respect to outward things, yet I am at times favored with a sustaining hope that He, whose mercies are over all His works, will not be altogether unmindful of Your afflicted Friend."

His eldest daughter, Elizabeth Marshall (1768-1836) now became the proprietress of the drug business founded by her grandfather some seventy years before, and under her able management, the business continued to increase, and was placed upon a firm financial basis. Probably she was the first woman in Philadelphia to embark upon a commercial career upon such an extensive scale, and she was the first American woman pharmacist of whom we have any knowledge. She continued to manage this business until 1825, when it was transferred to two of the apprentices, Charles Ellis and Isaac P. Morris.



ELIZABETH MARSHALL

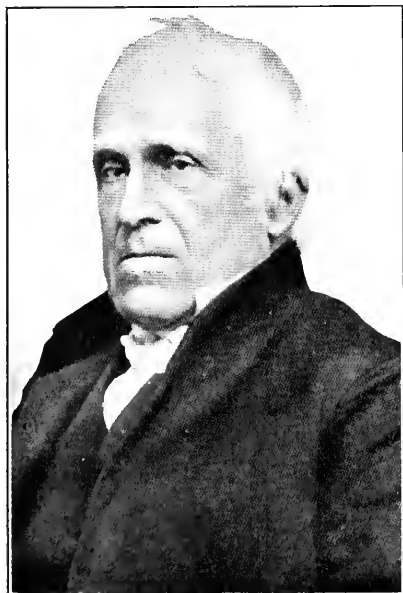
When the Philadelphia College of Apothecaries was founded in 1821, despite his advanced years, Charles Marshall was chosen President of the institution. For several years he gave the College his active interest and support. In 1824, by reason of the infirmities of his age, he resigned.

William Lehman was the first Vice-President of the College, serving in that capacity from 1821 to 1824. Upon the resignation of President Charles Marshall, he was elected to that office, and filled this position from 1824 to 1829. He was a cousin of Peter Lehman, one of the inaugurators of the movement that resulted in the founding of the College. He was educated in the University of Pennsylvania, graduating therefrom in both the literary course and in medicine, but he preferred to engage in the drug business with his father instead of practicing medicine. About 1802 he opened his own apothecary store at 97 South Second Street, and a few years later removed to 76 South Second Street (old numbers) below Chestnut Street. Here he was associated for awhile in partnership with William Smith, and later with Algernon S. Roberts. His father left him a moderate fortune, which he greatly increased by his efforts in the drug business. Despite the constant application required by the business, he continued to be an extensive reader and student throughout his life. He was a good Latin scholar, a fluent speaker of both French and German, and visited Europe on three different occasions.

He was elected to the Pennsylvania Legislature in 1814, and

was continuously re-elected to represent the City of Philadelphia for fifteen years. He was an earnest advocate of internal communications as the means of increasing the prosperity of his native city. William Lehman never married, he was happy in his devotion to the public causes which he had so much at heart, and gained a host of friends and supporters for these projects and was one of the most useful and eminent public men of his day. He died at Harrisburg on the twenty-ninth day of March, 1829, in the fiftieth year of his age. He left a bequest of \$10,000 to the Athenæum of Philadelphia for the purpose of erecting a suitable building, and this became the nucleus of the building fund through which they acquired their new hall, opened on October 18, 1847.

Daniel B. Smith. No history of American pharmacy would be complete without due reference and credit being given to this most learned and public-spirited pharmacist of his day, who was



DANIEL B. SMITH

remarkable for the versatility of his attainments. While characterized by a quiet and unostentatious manner, he was, nevertheless, a happy combination of business man, philanthropist, literary and scientific scholar, teacher, author and editor. In all of these activities he established an enviable reputation, and won the admiration of his contemporaries.

The ancestors of Daniel B. Smith were among those who established the early settlements in Burlington County, N. J. He was the son of Benjamin and Deborah (Morris) Smith, and he was born in Philadelphia in 1792. His father died when he was but

one year old, and his mother removed to Burlington, N. J.

His early education was acquired at the school of John Griscom, a highly esteemed educator who maintained a "Friends' school"



in Burlington, and whose reputation attracted scholars from Philadelphia, New York and portions of New England. In the fall of 1808, this Quaker schoolmaster gave a course of lectures on chemistry, and this was the first teaching of chemistry in the common schools of the United States of which we have any record. The influence of a teacher so enthusiastic and endowed with such natural qualifications, and gifted with a conversational ability that was magnetic, must have been a potent factor in deciding the choice of a business career for Daniel B. Smith, which would bring him into close association with scientific studies. After leaving the school, he entered the store of John Biddle on Market Street, between Fourth and Fifth Streets, Philadelphia, to learn the drug business. After completing his apprenticeship, a partnership existed with his preceptor under the firm name of Biddle & Smith for about one year. In 1819, Daniel B. Smith established his own store at the northeast corner of Arch and Sixth Streets. At that time this locality was the quiet, secluded, residential section occupied by many of the prominent members of the Society of Friends.

He was one of the organizers of the Apprentices' Library in 1820, for "the purpose of supplying wholesome instruction and useful reading for boys learning a trade." He was an active, if not the dominating spirit, in the founding of The Philadelphia College of Pharmacy, and was elected Secretary; after serving as Secretary for seven years, he was elected Vice-President in 1828, and President in 1829. For a period of twenty-five years, during a most trying period in the history of the College, he held this position, resigning in 1854.

When the Committee on Publication was appointed in June, 1825, the College having "in contemplation" to publish an occasional journal, containing improvements of formulas, new discoveries, and other interesting pharmaceutical information, Daniel B. Smith was appointed the chairman. When the first number of the journal of The Philadelphia College of Pharmacy<sup>4</sup> appeared in December, 1825, Daniel B. Smith was the editor and the author of the initial original article on "Epsom Salts and Magnesia." To him belongs the credit of having established from its inception, the journal on a high scientific and ethical plane.

<sup>4</sup> Under this title the publication was continued for six volumes; since 1835, it has been published under the more comprehensive name of THE AMERICAN JOURNAL OF PHARMACY.

He contributed a number of the articles to the first edition of the *United States Dispensatory*, and it was the intent of the authors, Drs. Wood and Bache, that he should prepare the pharmaceutical portion, but his removal to Haverford at this time rendered such a program impractical. Dr. George B. Wood publicly recorded his tribute to Mr. Smith's attainments in science and literature, as well as his appreciation of the services he had rendered in behalf of pharmacy.

In 1828, William Hodgson, Jr., who had learned the apothecary business in the store of Jacob Bell in London, became associated with Daniel B. Smith, and the firm of Smith & Hodgson continued to extend their manufacturing and wholesale drug business. A four-story building temporarily met the demands for increased room for manufacturing purposes, and subsequently this firm decided to engage exclusively in manufacturing at their new laboratory that they had erected on Grays Ferry Road, and in 1849 disposed of their drug business to two of their apprentices, Charles Bullock and Edmund A. Crenshaw.

Daniel B. Smith took an active interest in the notable discoveries in physics and chemistry, and repeated many of the published experiments. He became a member of the Franklin Institute soon after its organization in 1824. He was elected a member of the American Philosophical Society in 1829, and was also a member of the Academy of Natural Science. He was one of the inaugurators of the Historical Society of Pennsylvania, and that society's first Corresponding Secretary. He was one of the incorporators of the Philadelphia Savings Fund, and also of the institution known as the House of Refuge.

While science and philanthropy claimed much of his time, achievements in the field of general literature were equally attractive. In 1834 he accepted the chair of Moral Philosophy, English Literature and Chemistry in Haverford School (now Haverford College), and removed to Haverford. During his twelve years' residence here, he wrote "The Principles of Chemistry," a text book that went through two revisions. His lectures on "Ethics and the Lives and Doctrines of the Early Members of the Society of Friends" are spoken of as literary productions of great merit.

In 1846 he resigned from Haverford College, that he might give his attention to his increased drug business.

When the American Pharmaceutical Association was organized

in 1852, his prominence and accomplishments were recognized, and he was elected as the first President. He retired from active business in 1853. The last years of his long and useful career were quietly spent at his home in Germantown, where his life ceased on March 29, 1883, in the ninety-first year of his age.

Henry Troth. Henry Troth was born at Woodstock, a plantation a few miles from Easton, Pa. He spent the first thirteen years of his life with his parents. About this time a number of relatives and neighbors moved up to Tioga County, intending to establish a colony in what was then considered a frontier, and the lad persuaded his parents to allow him to accompany the party. He remained with these friends three years, enduring many hardships, learning lessons from the great book of nature, and gaining an education in practical expediency and self-reliance unobtainable from text books. At the age of sixteen, his aspiration for improvement led him to Philadelphia, where he entered upon a five years' apprenticeship with Jeremiah Morris, to learn the drug business.



HENRY TROTH

Here he mastered the many details of the apothecary business, and acquired a fund of useful knowledge and made friends that were of great value in his subsequent business career as a wholesale druggist. He had not quite reached his majority when he formed a partnership with Edward Needles, a brother-in-law, and the wholesale drug firm of Henry Troth & Company was established on Market Street, below Seventh (old number 222). On January 1, 1823, Henry's younger brother, Samuel F. Troth, was admitted to the firm, and on February 1, 1826, Samuel purchased the interest of Edward Needles.

Henry Troth was active in the organization of the College and for more than twenty years thereafter, in its management. For thirteen years he was Vice-President, at a time when the President was seldom in attendance, and presided at the meetings with dignity and impartiality. He was always kind and courteous, and guided by the highest motives. He died on May 22, 1842.

Samuel P. Wetherill. When the Board of Trustees was first organized on March 27, 1821, Samuel P. Wetherill was chosen as chairman. He was a member of the firm of wholesale drug and color dealers located at 65 North Front Street. The Wetherill drug store was established at this location in 1762, and for years had the reputation of being one of the largest dealers in drugs in America. The handling of paints, dyes, glassware and technical chemicals became an important part of their commercial transactions. They were among the pioneers in American chemical manufacture, their original manufacturing laboratory having been established by Samuel Wetherill in 1776. On the site now occupied by The Girard Trust Company, at Broad and Chestnut Streets, Samuel Wetherill built a white lead plant, and the first white lead made in America was in 1804 by Samuel Wetherill & Son. This plant having been destroyed by fire, a new factory was built about 1810, at Twelfth and Cherry Streets.

Peter Williamson. Peter Williamson was one of the original body of druggists and apothecaries who convened in Carpenters' Hall to organize the Philadelphia College of Apothecaries and served as the secretary of that meeting. He was the son of Peter-Jessie and Mary Williamson, and was born in Philadelphia, September 6, 1795. He received his preliminary education at a Friends' Seminary. His inclinations led him to take up the drug business and he engaged with John W. Bryant, whose store was located at Second and Pine Streets, to learn the business.

At the early age of eighteen years, he entered into partnership with Dr. Joseph Klapp, and their store was located at the northeast corner of Second and Almond Streets. Dr. Klapp had an extensive medical practice, and Mr. Williamson possessed a natural adaptation for the apothecary business. The firm was quite prosperous, and for many years this continued as the leading drug store in the old district of Southwark. To accommodate the largely increased retail trade, and their specialty, furnishing of medical supplies to the shipping interests, increased facilities were secured by

erecting a larger store at 710 South Second Street. In 1845, he associated his son, Jessie Williamson, Jr., in the business under the firm name of Peter Williamson & Son. In 1854, the business was sold to Mr. James L. Bispham.

Mr. Williamson also served the College as first Secretary of the Board of Trustees in 1821. In February, 1874, he was elected first Vice-President, but after holding this position for only one year, he resigned on account of his age, and entirely withdrew from active participation in business and scientific pursuits.

In March, 1874, he founded the first scholarship in the College.

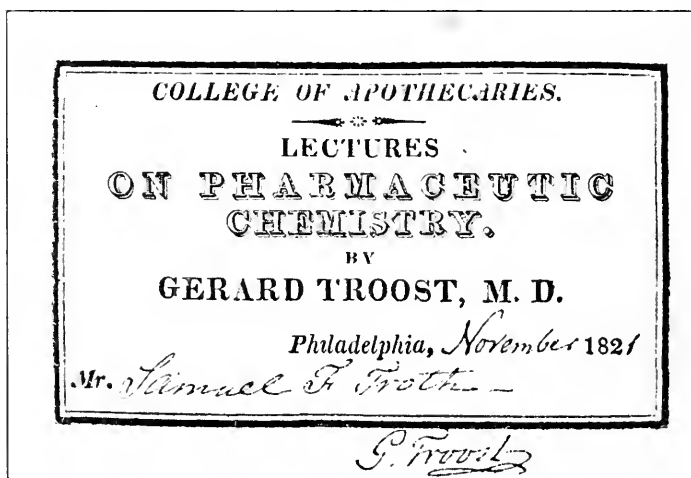
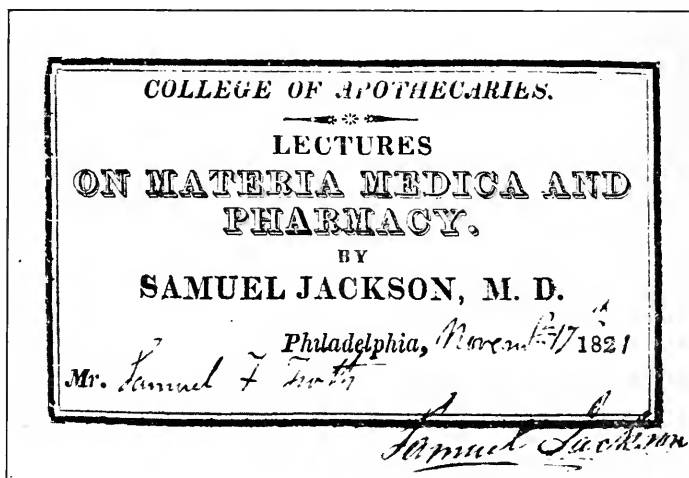
Mr. Williamson was active in Masonic circles; in the old volunteer fire department of the city, and in charitable works. He was one of the corporate members of the Trinity P. E. Church, and for twenty years was Rector's Warden. He passed away at his residence on the 6th of March, 1886, in the ninety-first year of his age.



PETER WILLIAMSON

The first meeting of the Trustees was held in Carpenters' Hall, on March 29, 1821. An organization was effected, with Samuel P. Wetherill as chairman, and Peter Williamson as Secretary, and a committee was appointed to take into consideration the subject of establishing a school of pharmacy, and to draft by-laws for the government of the Board of Trustees. On April 9th, an adjourned meeting of the Trustees was held, at which the Committee on By-laws for the government of the Board presented a draft, which was adopted, and the Committee on the School of Pharmacy reported a plan recommending lectures on Materia Medica and Pharmacy and on Pharmaceutical and General Chemistry. Those on Materia Medica and Pharmacy to be given on three

nights per week, from November 1st to March 1st, and those on Pharmaceutical and General Chemistry from March 1st to June 1st. The price for the tickets for the course on Materia Medica



ORIGINAL LECTURE TICKETS

and Pharmacy was fixed at \$15, and for the Chemistry course at \$12. In addition a matriculation fee of \$5 was to be paid by each student. The lecturers were to receive all of the emoluments from

their respective courses. At a meeting held a week later, the price for the tickets was changed, and it was agreed that for the first course the price was to be \$12, and for the second course \$10.

The following week, April 23, 1821, Samuel Jackson, M.D., was elected Professor of Materia Medica and Pharmacy, and Gerard Troost, M.D., Professor of Chemistry.

Dr. Samuel Jackson. Samuel Jackson, M.D., the first Professor of Materia Medica and Pharmacy, was born in Philadelphia on March 27, 1787. His father was a druggist, engaged in business on North Fourth Street, and Samuel learned the apothecary business there, and although he had been graduated a Doctor of Medicine from the University of Pennsylvania, he was active in pharmacy at the time of the founding of the College, and became one of its charter members.



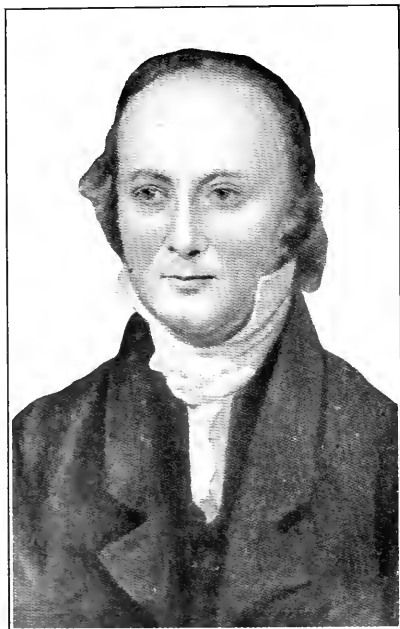
DR. SAMUEL JACKSON

He was eminently fitted for this professorship. His introductory lecture on "Conditions of Medicine in the United States, and the Means to Their Reform," evidenced the high ideals of the lecturer and forshadowed his future successful career as a medical practitioner and teacher.

In 1827, Dr. Jackson resigned his professorship in the College in order to assume a chair in the Medical Department of the University of Pennsylvania, with which institution he was connected as a teacher for thirty-six years. He played no insignificant part in the development of medical education. After his withdrawal from the chair of Materia Medica and Pharmacy, he did not lose his interest in the College of Pharmacy. He served as second Vice-President—1827-1829, and as first Vice-President—1829-1831. He died April 4, 1872, at the age of eighty-five years.

Gerard Troost, M.D., the first Professor of Chemistry, was

educated in Holland, both in medicine and pharmacy. Geology and mineralogy were his favorite studies, but all of the natural



DR. GERARD TROOST

sciences claimed his general interest. He was one of the founders of the Academy of Natural Sciences, and its first President. He likewise held the position of Mineralogist to Peal's Museum, a famous collection of natural objects, paintings and curiosities of many kinds, at that time exhibited on the second floor of the State House, over Independence Hall, and afterwards in the Arcade on Chestnut Street, above Sixth, where it was for many years one of the places for sight-seers in Philadelphia. The class was small, and despite his scientific attainments, Prof. Troost lacked ability as a teacher and failed to interest his students in his sub-

jects. This was largely due to his foreign accent, which made it difficult for the students to understand him. He served the College as professor for one year only, and later was elected Professor of Chemistry, Geology and Mineralogy in the University of Nashville, and his valuable reports as a State Geologist of Tennessee are considered the best works of his life.

On July 22, 1822, Dr. George B. Wood was elected Professor of Chemistry to fill the place made vacant by the resignation of Prof. Gerard Troost, and served the College in this capacity until 1831, when he was transferred to the chair of Materia Medica and Pharmacy, made vacant by the decease of Dr. Benjamin Ellis.

The following copy of the letter written by Dr. Wood to his mother soon after his appointment to the chair of Chemistry, the



original of this letter is preserved in the College of Physicians and Surgeons.

"Philada., 8th mo. 10, 1822.

"My dear Mother,

"Thou wishes to know something about my professorship. The Apothecaries of the city, the most respectable of them at least, have united to establish an institution for the instruction of their apprentices in the principles of their business and have obtained a charter from the state legislature, under the name of the *College of Pharmacy*. In this College there are two professorships, one of *Materia Medica*, the other of *Chemistry*—to the last of which I was chosen on the 23rd of last month by a vote of 11 out of 15 Directors. I shall deliver a course next winter to commence on the 1st of November and expect to have about 30 apprentices to attend, with, perhaps, some others. I calculate that the place will be worth to me at least 200 dollars. The preparation of this course is one thing that has been occupying a good deal of my time lately, etc., etc.



DR. GEORGE B. WOOD

"Thy affectionate son,

"GEO. B. WOOD.

"To Elizabeth Wood,

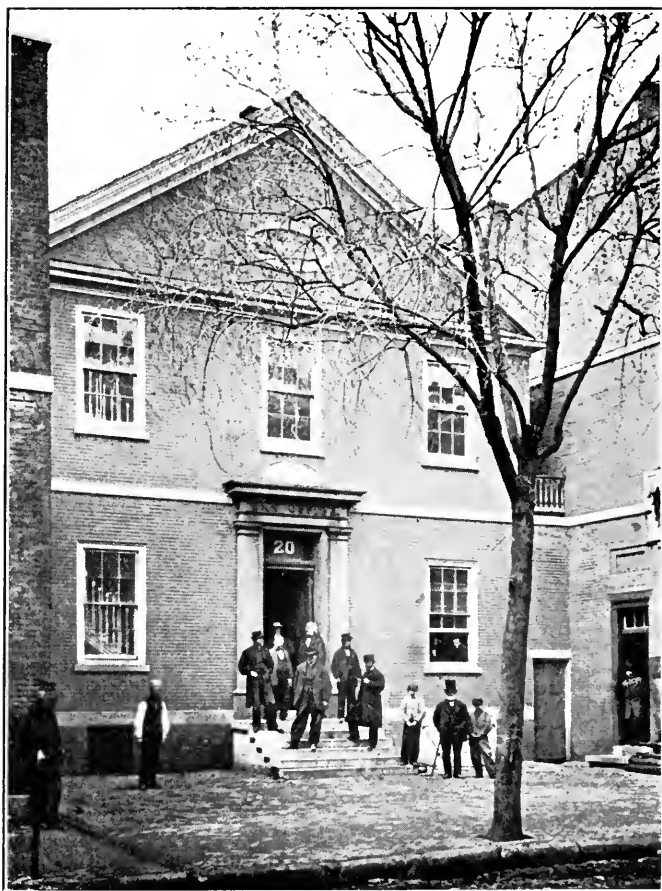
"Greenwich,

"Cumberland Co.,

"New Jersey."

The services of Dr. Wood in behalf of pharmaceutical and medical education belong to a subsequent period in the history, and we must reserve treatment of this subject for another occasion.

There still remained the selection of a suitable place for giving the instructions, and on July 23, the Board authorized the renting of the German Hall, situated on the west side of Seventh Street, south of Market, for lecture purposes, at an annual rent of \$200. This was the first home of the College, and instructions were given here until 1833.



GERMAN HALL

In Poulson's *American Daily Advertiser*, Monday, October 29, 1821, appeared the following advertisement :

#### COLLEGE OF APOTHECARIES

In the division of the sciences that characterizes the philosophy of the present age, and which has so much tended to their improvement, Pharmacy has been withdrawn from the charge of the Physician, and consigned to the care of the Apothecary. In Europe, this division has long been recognized and sanctioned by the Medical Profession. Colleges of Apothecaries, and other similar institu-

tions, have been established, devoted expressly to instruction in Pharmacy and its subsidiary sciences. On the continent, most of the respective governments have prohibited, under heavy penalties, any one from selling or preparing Drugs and Medicines for administration, who has not passed through a course of instruction, and become practically acquainted with the business. In Great Britain, most Apothecaries are regularly instructed, by attendance on the lectures of the Colleges of Apothecaries of London and Dublin, and are associated as members, while abuses in the business are guarded against by severe penalties, enacted by Parliamentary statute.

In this country, Pharmacy has been entirely neglected, as a science. Previous instruction has not been considered indispensable, in order to capacitate an Apothecary for pursuing his profession, while very few practitioners of Medicine possessed more than a superficial acquaintance with the principles and details of Pharmaceutical knowledge. From this state of things, many evils, some of a serious and aggravated nature, have flowed, urgently requiring correction.

Many Apothecaries of this city have long been sensible of the necessity of taking some efficient measures, by which the irregularities and abuses that have crept into their business, should be abolished; and that their profession should be placed on that respectable footing to which it is entitled, by its usefulness to society, and as an important branch of the science of Medicine. With these views, they have founded the PHILADELPHIA COLLEGE OF APOTHECARIES.

This institution has already established many wholesome regulations for the government of its members, calculated to inspire confidence in all those who are attached to it; and has provided for a course of public instruction, under its auspices, in *Materia Medica* and Pharmacy, and Pharmaceutical Chemistry, with the intention of adding, ultimately, other collateral sciences. A Cabinet is also forming, of choice and selected specimens of Drugs and Medicines, of the best qualities.

An institution embracing so many objects of high importance and utility to the Medical Profession, and the public generally, and so well calculated to perfect those objects, cannot fail to meet the approbation and support of the liberal and well-informed practitioner, and every member of society.

The College announces, that the Course of Lectures will com-

mence in the first week in November, and will be delivered three times a week, in the evening, during the winter, in the Hall of the German Society, south Seventh Street.

Lectures on Materia Medica and Pharmacy, by DR. SAMUEL JACKSON.

Lectures on Pharmaceutic Chemistry, by DR. GERARD TROOST.  
By order of the Board of Trustees.

PETER WILLIAMSON, *Secretary*.

And in Poulson's *American Daily Advertiser*, Tuesday, November 6, 1821, the following:

#### PHILADELPHIA

#### COLLEGE OF APOTHECARIES

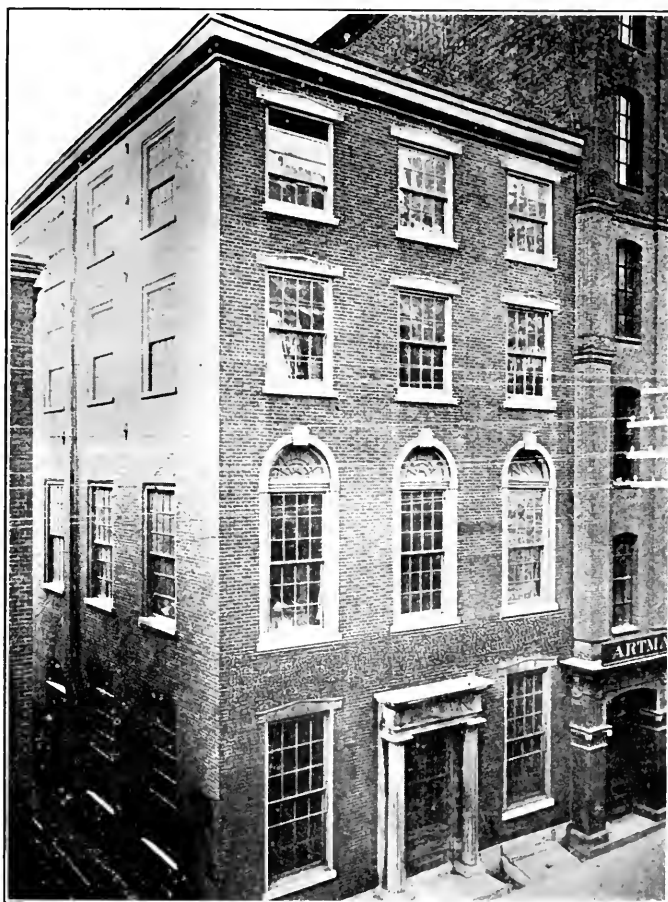
The Introductory Lecture to the course on Materia Medica and Pharmacy, will be delivered by SAMUEL JACKSON, M.D., on Friday evening, November 9th, in the German Society's Hall, in South Seventh Street, between Market and Chestnut; and

The Introductory Lecture, to the course of Pharmaceutic Chemistry, will be delivered by GERARD TROOST, M.D., on Saturday evening, November 10th, at the same time and place.

On March 21, 1822, at the suggestion of William Lehman, a resolution was adopted, changing the name of the College to a more appropriate title, The Philadelphia College of Pharmacy, and under this name it was incorporated on March 30, 1822.

During the early part of 1829, the German Society, desiring the rooms occupied by the College, and the members feeling that the time had now arrived when the College should carry out one of its original purposes to own a permanent home, a committee was appointed, July 20, 1829, to report on a permanent situation for the College. The attempt to secure a site from the Trustees of the University of Pennsylvania, on ground rent, of a lot on Seventh Street, above Market, having failed, the committee reported, on November 21, 1831, that "two sites for the purpose can be obtained, one site at the S. W. corner of Marble and Tenth Streets, running East and West between Market Street, containing a frontage of 38 feet on Tenth Street, and running to a depth of 60 feet, to a 6 foot wide alley, thus presenting a frontage on three sides. The price asked is \$8,000. The whole extent of the lot is 96 feet on Tenth

Street, running back 92 feet, and the asking price is \$20,000. As a matter of speculation, it would be profitable to purchase the whole lot, but in the opinion of your Committee it is too heavy a concern to enter into.



ZANE STREET BUILDING.  
 HOME OF THE COLLEGE, 1833-1868

"The second site is on the South side of Zane Street, adjoining Six's Sugar House, which is bounded on the West by at least a 10 foot alley, on the South by a vacant lot, which is to continue always opened, thus presenting three fronts, which is desirable on account of light. The lot is 30 feet on Zane Street (now Filbert

Street), running to a depth of 46 feet. The price asked is \$200 per annum on irredeemable ground rent, or if redeemed in ten years such a capital sum as will produce \$200 per annum, and in either case will expect \$1000 for the buildings now on the lot, making a sum total of \$4,333.33. It is the opinion of your Committee that this lot should be purchased, and no doubt Abraham Miller, the owner, will allow some reduction in the price of the buildings." The committee was authorized to offer Abraham Miller \$225 per annum for the lot, the ground rent redeemable in twenty years, for the sum of \$4,500, and the committee further authorized to obtain subscribers to a loan at 6 per cent. interest for the purpose of erecting a building on the said lot.

Abraham Miller, having accepted the above offer, the committee was directed to proceed with the erection of the building, and in 1833, the College erected a four-story building, with a frontage of 30 feet wide and a depth of 46 feet. The first and second stories were built with high ceilings for lecture rooms, in an amphitheater arrangement. This modest first home owned by the College was erected at a cost of \$8,323.74.

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## STUDIES ON THE CASSABA AND HONEY DEW MELONS.\*

By HEBER W. YOUNGKEN, PH.D.

During the late autumn and winter of recent years the writer has noticed in a few of the local markets two luscious fruits which dealers sold under the name of "Cassaba" and "Honey Dew Melons," or by the collective name of "Winter Melons." Their general external appearance indicated that they were fruits of the *Cucurbitaceae*, but inquiry in the local market failed to elicit information as to their botanical origin and history. The only data procurable from this source was to the effect that they came from California and Colorado respectively, and were of excellent keeping quality.

The scant references to these melons in American and English works on horticulture were far from satisfying, and prompted this

\* Read at meeting of Pennsylvania Pharmaceutical Association, Harrisburg, Pa., June 24, 1920.

investigation into their origin, history, structure and chemical constitution.

Both of these melons undoubtedly belong to the group which Bailey in his "Standard Cyclopedia of Horticulture" calls the *Inodorous* variety of *Cucumis melo*.

*Cucumis melo*, the progenitor of these forms, is a rough, hairy, annual herb which like many other plants of the gourd family is capable of clinging to supports and climbing, through the possession of tendril-bearing stems. The leaves are subcordate and palmately-lobed, the lobes being irregularly toothed. They arise from the stems in about the same plane as the tendrils. Both



Fig. 1. End view of Cassaba and Honey Dew Melons. Cassaba to left. Honey Dew to right.

staminate and pistillate flowers are borne on the same plant, usually, but in some forms hermaphrodite flowers also occur. In all cases the flowers are axillary. The calyx is campanulate with a 5-toothed limb. The corolla is campanulate, 5-lobed, with lobes somewhat fringed. The 3 stamens with short, thick filaments are inserted at the base of the corolla. The gynoecium is composed of three syncarpous carpels, the ovarian portion being inferior and 3 celled, the style short and 3-fid. The ovules are numerous, several-seriate, horizontal and anatropus. The fruit is a pepo with numerous horizontal, compressed and ex-albuminous seeds.

According to Naudin,<sup>1</sup> who carried on investigation and experiments with about 2000 living plants, this species possesses an extraordinary number of varieties and breeds. The varieties, moreover, can be fertilized by each other and yield varied and variable

products. They are classed by him into ten groups which he terms: canteloups, melons, brodes, sucrons, melons d'hiver, serpents, forme de concombre, Chito, Dudain, rouges de Perse, and sauvages, each of these groups containing varieties or nearly allied races.

According to the same authority the species is indigenous to Southern Asia from the foot of the Himalayas to Cape Comorin.

De Candolle,<sup>2</sup> however, thinks that *Cucumis melo* like *Citrullus Colocynthis* was once wild from the west coast of Africa as far as India.

The Egyptians grew it and the Romans and Greeks were at least familiar with some of its varieties.<sup>3</sup> Columella, of Gades, a contemporary of Seneca, an extensive writer on agriculture who flourished about the middle of the first century A. D., refers to a variety known as the serpent melon in the phrase *ut coluber . . . ventre cubat flexo*. Pliny in his writings refers to the melons as pepones.



Fig. 2. Lateral aspect of Cassaba (to left) and Honey Dew (to right) Melons.

Its introduction into China appears to date from the eighth century.

In 1597, Gerard,<sup>4</sup> in his Herbal, described and figured several kinds of melons. But it was not until 1629, according to Oliver de Serres, that they began to be cultivated on a large scale in France.

Some of the valued modern types of the species, such as the Cantaloupes, Dudain, Pineapple Melons and Netted Melons had their origin in Persia and the neighboring Caucasian regions. From here they were introduced into the Mediterranean countries, not-



ably Asia Minor, Italy, France and Spain, whence their seeds were conveyed to this country.

The variety *inodorus*, which yields fruits known as winter melons, is said by Bailey <sup>5</sup> to differ from the wild species in having lighter colored, less hairy and narrower leaves, and little or none of the muskmelon odor which characterizes the fruit of the latter.

#### HISTORY OF THE CASSABA AND HONEY DEW MELON.

The Cassaba Melon, also termed "Kassaba," "Casaba," "Casabad" and "Casba," was named from the town of Kassaba, about 15 or 20 miles from Smyrna where it was extensively grown and whence it was introduced to this country. Late in 1878 Dr. J. D. B. Stillman and James L. Flood, who found these melons in the hotels of Smyrna, sent seed to California. In the following year (1879) the first crop was grown in that state.



Fig. 3. Cassaba Melon cut crosswise to show internal appearance.

Hundreds of acres are now grown each year in the San Fernando valley of Southern California. They are shipped to the markets of this country mainly in October, November and December.

The Honey Dew Melon is an old South of France variety of the Winter Melon renamed. Vilmorin, of Paris, has listed it for a number of years under the name of the White Antibes Winter Melon. At the present time it is extensively grown in Colorado.

Dreer's Garden Book for 1919, p. 8, states that it is suitable for growing in all places of equal latitude to Philadelphia and the West, including California.



Fig. 4. Honey Dew Melon cut transversely to show internal appearance.

While both of these melons have been well known to and used by the Europeans for many years, they appear, up to the present, to be little known, and only of limited use in the United States. Their rich honey-like flavor, with far more succulence and longer keeping qualities than muskmelons should commend them to all seeking substitutes for cantaloupes and muskmelons during the autumn and winter season, and bid fair for their more extensive future production in this country.

#### GROSS STRUCTURE OF THE CASSABA MELON.

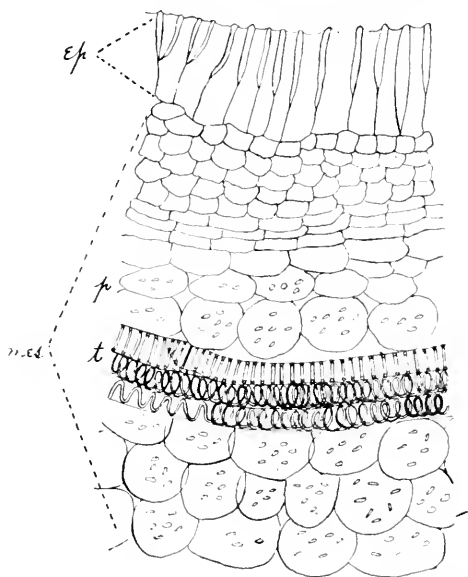
This fruit (Fig. 1) is of large broadly oval shape from 6, 8 to 9 inches long and 4 to 6 inches in thickness. Its outer skin is yellow and shows numerous irregular longitudinal grooves and wrinkles (Fig. 2). When cut (Fig. 3) it exhibits a thick, whitish flesh one and one-quarter to one and one-half inches thick and a comparatively small seed cavity. In the seed cavity are to be observed 5 placentas, each bearing numerous flattened, ovate light-yellow seeds 10-12 mm. long. The hilum is near the pointed end. The cotyledons are plano-convex, white and oily. The radicle is short and conical. The taste of the fruit is cantaloupe-like; that of the seed, bland.

# HISTOLOGY OF THE CASSABA MELON.

This fruit, being the product of the ripening of the combined receptacle and inferior ovary, presents for microscopical examination two distinct regions, viz., pericarp (receptacle and ovarian wall) and seed.

## PERICARP (FIG. 5).

1. The *pericarp* in surface view shows numerous for the most part polygonal cells, the vertical walls of which are considerably thickened. Scattered through this region are abundant stomata whose guard-cells are surrounded by 5 more or less crescent-shaped neighboring cells (Fig. 6). The walls of the stomatal apparatus are colorless. In transverse view the epicarp cells (Fig. 5), are palisade-like and form a layer up to 80 microns thick. The outer



**Fig. 5.** Transverse section of portion of pericarp of Cassaba Melon. Epicarp with rod-thickenings in the radial walls (ep); mesocarp (mes); pitted parenchyma (p); spiral tracheae (t), (magnified).

half of most of the vertical walls of these cells is greatly thickened, while the inner half is for the most part thin walled. Occasionally thickening of the vertical wall extends nearly or quite the complete length of the cell.

A considerable number of uniseriate non-glandular hairs, up to

243.2 microns in length are to be observed as outgrowths of the epicarp. Each of these (Fig. 7) is composed of 4-5 cells. The basal cell of the hair is characterized by an irregular thickening of its wall, while the distal cell shows a curved, sharp-pointed summit. Numerous circular scars are also evident in this region. (See Fig. 6A.) These represent the bases of the non-glandular hairs which have become detached. The epicarp cells bordering upon them are arranged in radiate fashion.

2. The *mesocarp* (Fig. 5 mes.) is composed of a matrix of fundamental parenchyma whose walls are characteristically pitted. The parenchyma cells are smallest in the outer regions, but gradually increase in size toward the endocarp. The intercellular-air-spaces are also the largest in the inner part of this region. Coursing through the mesocarp are numerous fibrovascular bundles of the bi-collateral type with prominent sieve tubes and spiral tracheae. The latter may attain a diameter of 25.66 microns. Accompanying the bundles, especially in the inner regions, will be observed numerous branching and anastomosing lacticiferous vessels.

3. The endocarp adheres to the seeds as a thin membrane.

#### SEED (FIG. 8).

1. *Spermoderm*, consisting of (1) a *palisade epidermis* (ep) with longitudinal ribs strengthening the radial walls. These are slender and unbranched and up to 156 microns in length. The cells of the

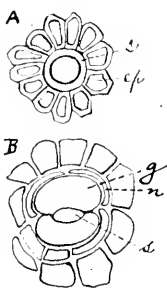


Fig. 6. A. Circular scar (s), representing base of non-glandular hair detached from epicarp of Cassaba Melon. Note the epicarp cells (ep) arranged around it in radiate fashion. B. Stomatal apparatus of epicarp of Cassaba Melon. Stoma (s); guard cells (g); neighboring cells (n), (greatly magnified).

epidermis contain a number of small spheroidal to angular starch grains. Upon coming in contact with water their outer walls, consisting of a mucilaginous modification of cellulose, are changed to mucilage.

2. *Sclerenchyma*, a zone of 3 to 4 layers rounded to ovate stone cells with radial pore canals. The inner layer of these cells becomes elongated toward and at the edges of the seed.

3. A zone of one or two layers of spherical to oval-shaped cells whose walls show reticulate markings.

4. A zone of about 4 layers of *spongy parenchyma* cells.

5. An inner epidermis of tangentially-elongated cells.



Fig. 7. Non-glandular trichome found on epicarp of Cassaba Melon (greatly magnified).

II. *Persiperm*. A prominent yellowish band (n) of tangentially-elongated cells, constituting the remains of the nucellus.

III. *Endosperm*. A layer of aleurone cells (al).

IV. *Embryo*, showing two plano-convex cotyledons and a small conical radicle toward the micropylar end of the seed. Each cotyledon (cot) in cross section shows an epidermis (e) of small clear cells, 2 to 3 layers of palisade cells (pal) (the broadest zone being toward the center), and several layers of spongy parenchyma (s). Sections cut through the center of the cotyledon show 3 fibrovascular strands coursing lengthwise through the spongy parenchyma. Both palisade and spongy parenchyma cells contain a large number of fixed oil droplets and aleurone grains 2 to 6.4 microns in diameter.

#### GROSS STRUCTURE OF THE HONEY DEW MELON.

This fruit (Figs. 1 and 2) is of large round to oval shape, from about 5 to 7 inches long and 4 to 5 inches in diameter. Its outer skin is hard, smooth and whitish. When cut, it exhibits a thick, greenish flesh (sarcocarp) up to one and one-quarter inches in thickness. The flesh is of a sweeter and richer flavor than that of the Cassaba melon. The seed cavity in the center differs from that of the Cassaba by showing only 3 placentæ (Fig. 4). Each of these bear numerous compressed ovate to ovate-lanceolate light yellow seeds 12 to 13 mm. long. These become shiny when placed in water, due to the formation of mucilage by the outer layer of cells of the seed coat. Other microscopic characteristics of the seed resemble those described under the Cassaba melon.

## HISTOLOGY OF THE HONEY DEW MELON.

Alike with the fruit of the Cassaba, this melon presents for examination pericarp (ripened receptacle and ovarian wall) and seed regions.

## PERICARP (FIG. 9).

1. The *epicarp* (ep.) in surface view shows for the most part polygonal cells which are strikingly similar in nature to those of the Cassaba melon. The stomata are likewise numerous, but their

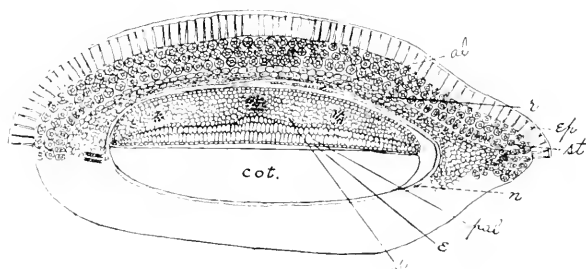


Fig. 8. Cross section of seed of Cassaba Melon (semi-diagrammatic), showing palisade epidermis (ep); sclerenchyma zone (st); reticulated parenchyma (r); perisperm (n); endosperm (en); cotyledons (cot); epidermis of cotyledon (e); palisade parenchyma (pal); and spongy parenchyma (s). Note the three strands of fibrovascular tissue extending through the spongy parenchyma region, as indicated by groups of circles (greatly magnified).

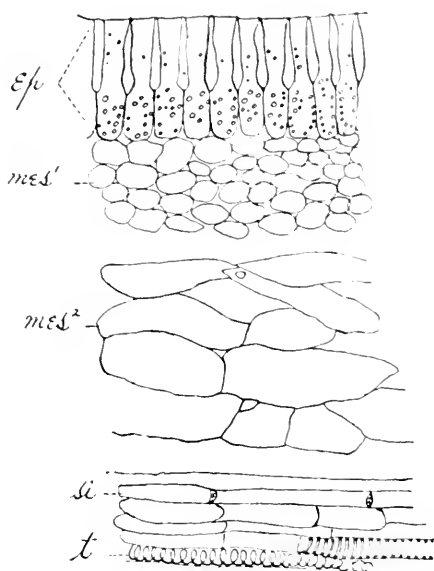
guard cells are surrounded by 6-8 irregular shaped neighboring cells. Circular scars of non-glandular hairs are to be observed in the mature fruit which have a diameter of from 35.2 microns to 41.6 microns with a lumen varying from 9.6 microns to 11.2 microns. In cross section the epicarp cells are found to be palisade-like, thickened along their radial walls for half or more of their length and up to 105 microns high. These cells possess numerous small rounded starch grains.

2 and 3. The *mesocarp* and *endocarp* are quite similar in structure to the same regions of the Cassaba Melon.

## SEED (FIG. 11).

1. *Spermoderm*, consisting of (1) a palisade epidermis which readily separates from the subjacent layers upon coming in contact with water. These cells are 105 microns long and show longitudinal ribs strengthening the radial walls; (2) sclerenchyma, a zone of 2

to 4 layers of stone cells having thick walls that are pierced by numerous pore canals. In surface view these cells are elongated and show wavy walls which are perforated by distinct pores of an angular to rounded outline (Fig. 12).



**Fig. 9.** Transverse section through representative portions of the pericarp of the Honey Dew Melon. Epicarp (ep); outer region of mesocarp showing parenchyma cells of ripened receptacle (mes¹); inner region of mesocarp, composed of parenchyma cells of ripened ovarian wall (mes²); sieve tubes (s) and spiral tracheae (t) of a bi-collateral bundle (greatly magnified).



**Fig. 10.** Portion of surface section of epicarp of Honey Dew Melon. Note guard cells are surrounded by 7 irregular shaped neighboring cells. The regular epidermal cells are outside of these (highly magnified).

3. A layer of pitted cells (p).
4. One to two layers of reticulated parenchyma (r).
5. A layer of large parenchyma cells (l).

6. A narrow zone of collapsed spongy parenchyma.
7. An inner epidermis of thin-walled tangentially-elongated cells.

II. *Perisperm*. A distinct yellowish band of compressed cells (n).

III. *Endosperm*. A layer of aleurone cells (al.) with aleurone grains up to 6 microns in diameter.

IV. *Embryo*. Similar in structure to that of the Cassaba.

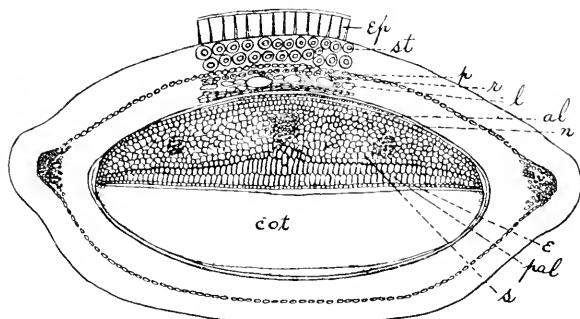


Fig. 11. Cross section of seed of Honey Dew Melon (semi-diagrammatic). Epidermis (ep); sclerenchyma zone (st); pitted cells (p); reticulated parenchyma (r); large parenchyma cells of spermoderm (l); perisperm (n); endosperm (al); cotyledons (cot); epidermis of cotyledon (e); palisade tissue (pal); spongy parenchyma with 3 fibrovascular strands (s), (magnified).

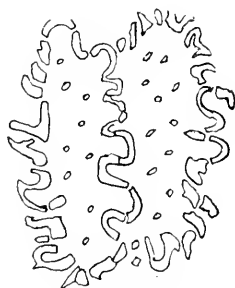


Fig. 12. Surface view of stone cells of spermoderm of Honey Dew Melon (greatly magnified).

#### CHEMISTRY OF FRUITS.

The following chemical analysis of the fruits was made by Prof. Charles H. La Wall and Mr. Joseph W. E. Harrison, to whom the author expresses grateful acknowledgment:



	Honey Dew Melon	Cassaba Melon
Total weight .....	1388.3 grams	3316.9 grams
Wt. of seeds and placenta ..	87. "	293. "
Wt. of rind .....	680. "	1360. "
Total refuse .....	767.4 "	1653. "
Amount of edible portion ...	45%	50%
Composition of pulp.		
Moisture .....	90.52%	89.05%
Ash .....	0.52%	0.80%
Crude fiber .....	0.36%	0.54%
Protein .....	0.51%	1.21%
Reducing sugar before inv. ..	2.05%	1.87%
" " after " ..	4.04%	2.76%
Fat .....	none	none

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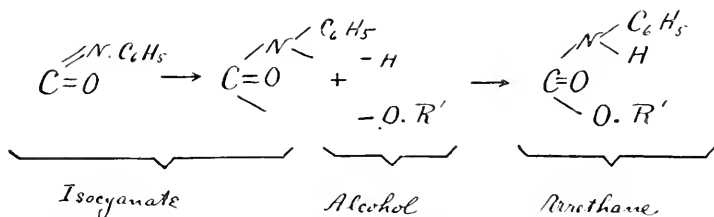
1. Annales des Sciences Naturelles, 4th ser., vol. 2, 1859.
  2. Origin of Cultivated Plants, by De Candolle, p. 261, 1885.
  3. Encyclopedia Britannica, ed. 2, vol. 18, p. 98.
  4. Herball, p. 772, 1597.
  5. Standard Cyclopedia of Horticulture, 3rd ed., vol. 2, p. 908, 1919.
- Botanical Research Laboratory.  
 Philadelphia College of Pharmacy and Science.  
 June 21, 1920.

## URETHANES OF THYMOL AND CARVACROL.

By D. C. L. SHERK.

### PHENYL URETHANES.

The preparation of urethanes is an addition reaction between an alcoholic hydroxyl and an isocyanate. The reaction takes place in this manner:



forming an ester of carbamic acid,  $\text{NH}_2\text{CO.OH}$ . The urethanes have been widely used in the characterization of hydroxyl derivatives, primary, secondary and tertiary.

The phenyl derivative of thymol was prepared by Leuckart<sup>11</sup> by the action of phenyl isocyanate on thymol in the presence of aluminum chloride. Hoffman<sup>12</sup> had first obtained these products by heating the isocyanate and phenol at 100° for long periods of time in sealed tubes. The yields varied from 16 to 64 per cent. The use of aluminum chloride was an improvement. Goldschmidt<sup>13</sup> first mentions the preparation of the phenyl derivative of carvacrol by the use of aluminum chloride and suggests its usefulness as a method of identification. Weehuizen<sup>14</sup> simply heats the constituents with the isocyanate in slight excess, together in a petroleum hydrocarbon boiling about 170-200°. The urethane crystallizes out; while the components not reacting remain dissolved. This modification of the method requires no condensing agent, and heating at the boiling point for one-half hour is all that is necessary to cause the reaction to take place. The phenol is dissolved in 10 parts of solvent; the isocyanate added in slight excess, and the mixture refluxed for one-half to one hour. The urethane crystallizes out on cooling and after filtering and washing with two small portions of the hydrocarbon it may be purified in the usual manner.

*Application to Thymol.*—An attempt was made to adapt the method to a somewhat larger scale of production than 1 gram. Accordingly, 5.28 g. of thymol with 4.6 g. phenyl isocyanate, representing a 10 per cent. excess, were introduced into an acetylation flask. The mixture became cold. To this were added 20 cc. petroleum (boiling 170-200°) and the mixture heated one hour. The cooled reaction mixture deposited crystals which were washed with two 5 cc. portions of petroleum and weighed. The yield was 6.75 g. or 71 per cent., with a melting point of 103°. Weehuizen<sup>14</sup> reports 106-107°; while the literature gives either 104° or 107° as the melting point. Crystallized once from alcohol (95 per cent.) it melts at 106°, a second crystallization raises this to 106.5-107°. It does not crystallize well from benzene on cooling, and does not precipitate on addition of heptane.

The determination of nitrogen by the Kjeldahl method pre-

<sup>11</sup> Leuckart, J., *pr. Chemie*, II, p. 320.

<sup>12</sup> Hoffmann, *Ber.*, 4 (1871), p. 249.

<sup>13</sup> Goldschmidt, *Ber.*, 26 (1893), p. 2086.

<sup>14</sup> Weehuizen, *Rec. trav. Chim.*, 87 (1918), p. 266.

sented some difficulties. Direct digestion with potassium sulphate yielded only very uncertain results. Copper sulphate added as in IV gave even less satisfactory results.

I.	5.5464 g.	required	22.63 cc	N/10 HCl.
II.	0.5146 g.	required	13.11 cc	N/10 HCl.
III.	0.3696 g.	required	11.72 cc	N/10 HCl.
IV.	0.2934 g.	required	0.90 cc	N/10 HCl.
				Found                      Theory for $C_{17}H_{19}NO_2$
				5.20 p. c.
Nitrogen	I.	5.80 p. c.		
	II.	3.35 "		
	III.	4.44 "		
	IV.	0.47 "		

On a basis of yield, method of preparation, and melting point determination the substance was certainly thymol phenyl urethane and the nitrogen determination was not checked by Dumas' method for this compound.

*Application to Carvacrol.*—5.04 g. carvacrol treated in the same way as thymol and run in parallel yielded 7.77 g. urethane, or 86 per cent. This melted originally at  $134.5^\circ$  to  $136^\circ$ . Crystallized from alcohol (95 per cent.) is melted at  $138^\circ$ . Further crystallization from alcohol did not raise this value. The hot benzene solution sets to a mush on cooling and the product melted at  $133.5$  to  $134.5^\circ$ . Addition of an equal volume of heptane to these mother-liquors gave a copious deposit of crystals melting this time at  $138^\circ$ .

It was found impossible to raise the melting point to  $140^\circ$ , as has been claimed by Gildemeister<sup>15</sup> for this substance; even though it had been treated with the following solvents: alcohol, dilute alcohol, benzene and heptane.

Analysis by the Kjeldahl method using potassium sulphate and also with copper sulphate as in IV gave unsatisfactory results.

In order to confirm the composition of these substances nitrogen was determined by the Dumas method.

I.	0.3054 g.	yielded	14.9 cc	nitrogen at $22^\circ$ and 701 mm.
II.	0.2440 g.	yielded	13.5 cc	nitrogen at $24^\circ$ and 703 mm.
				Found                      Theory
I.		5.25 p. c.		5.20 p. c.
II.		5.53 "		

<sup>15</sup> Gildemeister, Arch. d. Pharm., 233 (1895), p. 188.

*Application to Hydrothymoquinone.*— Since hydroquinone<sup>16</sup> yields a diurethane, hydrothymoquinone was treated with two mols of phenyl isocyanate in slight excess and heated in petroleum, using 10 cc. per gram of phenol. The phenol melted on warming and gave a clear solution, which after about 15 minutes heating began to deposit crystals as spherules about 1 mm. in diameter. The cooled reaction mixture was filtered and refluxed again when a small quantity was recovered. For this preparation 2 grams of phenol were taken and the following recovery made:

Yield in grams	Per cent.	m. p.
4.765	81.6	229-230°
.095	1.6	210-220°

Another lot was prepared starting with 4 grams of phenol. When the isocyanate was added to this, reaction took place at once, even before dilution with petroleum or heating because a residue formed which later was found to be insoluble in the boiling reaction mixture. From this mixture 9.25 g. were recovered, representing a yield of 84 per cent.

These high yields indicate that both hydroxyl groups react and that a diurethane results. This is also wholly indifferent toward an alkali solution in the cold, indicating the absence of hydroxyl groups.

Analysis by the Kjeldahl method gave satisfactory results in this case.

I.	0.2936 g.	required	15.24 cc	N/10 HCl.
II.	0.3139 g.	required	15.23 cc	N/10 HCl.
		Found		Theory for $C_{24}H_{24}N_2O_4$
Nitrogen	I.	7.27 p. c.		6.93 p. c.
	II.	6.83 "		

However, to remove uncertainty as to the accuracy of this method, which seems to fail on the other urethanes, nitrogen was determined by Dumas' method.

I.	0.2302 g.	gave	15.8 cc	$N_2$ at 24° and 702 mm.
		Found		Theory
Nitrogen		7.36 p. c.		6.93 p. c.

<sup>16</sup>Snape, Ber., 18 (1885), p. 2429.

In sharp contrast with the solubility of the monoderivatives, the solubility of this product was slight. It is not soluble enough in benzene to allow this to be used for crystallization. In 95 per cent. alcohol it is slightly soluble in the hot and comes out as a fine powder. In ethyl acetate, chloroform, and carbon tetrachloride it is very slightly soluble; yet it separates in fine crystals from the acetate on cooling. Acetone dissolves it readily giving on evaporation hexagonal plates with one elongated axis. Ethyl acetate does not precipitate the acetone solution, while heptane does, and carbon tetrachloride gives a turbidity and a few crystals after warming.

For purification 14.0 g. of urethane were extracted under a reflux condenser with 190 cc. benzene for one hour. The residue was repeatedly extracted with 200 cc. 95 per cent. alcohol, crystallizing each time and repeating the extraction with the mother-liquor. After seven extractions 6.0 g. remained. This residue was extracted with 100 cc. ethyl acetate in the same manner three times, and finally the 4.0 g. remaining dissolved in acetone and recovered on evaporation.

Procedure	Turns brown	M. p.	Recovery	Total
Original .....	—	220–230°	—	14.0 g.
Benzene extraction .....	205°	213–216°	0.34 g.	
1st Alcohol .....	210°	229–229.5°	1.41	
2nd Alcohol .....	205°	226–227°		
3rd Alcohol .....	212°	227°	0.64	
4th Alcohol .....	200°	226.5–227.5°	0.69	
5th Alcohol .....	—	—	0.33	
Residue after this .....	210°	228–229.5°		
6th Alcohol .....	—	—	0.39	
7th Alcohol .....	—	—	0.58	
Remaining .....				5.93 g.
1st ethyl acetate .....	203°	224–226°	0.48	
2nd ethyl acetate .....	203°	225–228°	0.54	
3rd ethyl acetate .....	—	—	0.41	
Remaining .....				4.0

*Melting Point of Re-crystallized Product.*

Solvent	Turns brown	M. p.
Acetone 1st crop .....	223°	232–233°
Acetone 2nd crop .....	226°	232–233° gas evolved
Ethyl acetate, crystallized .....	223°	232–233°
Ethyl acetate, evaporated .....	220°	233°
Alcohol .....	213°	229–230.5° gas evolved

The product is thus practically pure as it separates from the reaction mixture. After extraction of the crystals with benzene to remove solvent they may be obtained pure by one crystallization from acetone or two from ethyl acetate.

$\alpha$ -NAPHTHYL URETHANES.

In the extension of this work to the use of  $\alpha$ -naphthyl isocyanate as a reagent the method of Weehuizen was used. There is one mention of the preparation of the carvacrol derivative. The same procedure was followed as in the other cases, for the phenol and isocyanate were heated together with petroleum in an acetylation flask. The yields with this reagent were not so good. Perhaps a greater solubility in the petroleum accounts for this because after separation of one crop of crystals and reheating only a very little more came down. With phenyl isocyanate the intensity of the odor was a gauge of the completeness of the reaction, but that advantage was lost here. To conserve the reagent the phenols were taken in slight excess in these reactions.

*Application to Thymol.*—2.00 g. thymol and 1.65 g. isocyanate were heated with 15 cc petroleum for 45 minutes. On standing over night nothing crystallized out even on scratching the walls of the flask. It was again heated for one hour and fifty minutes after which crystals appeared on cooling. The crystals appeared as radiating clusters or spherules and weighed 1.34 g., melting at 155°. The first crop from alcohol came out as clusters of needles, melting at 156-157°; while a further quantity recovered by dilution of the alcohol melted at 149-150.5°. On long standing the reaction mixture deposited a slight crust on the walls of the container. The yield is 43.0 p. c. From alcohol it forms felted masses of needle-like crystals, melting at 156-157°.

After the reaction mixture had been heated again and allowed to stand four weeks, only a very thin crust of crystals on the walls of the flask appeared.

An analysis of this compound by the Kjeldahl method, using copper sulphate, gave unsatisfactory results. Analysis by Dumas' method gave results agreeing with the theory.

I.	0.2338 g.	gave	10.9 cc	N <sub>2</sub> at 24° and 708 mm.
II.	0.1919 g.	gave	8.0 cc	N <sub>2</sub> at 24° and 707 mm.
III.	0.1806 g.	gave	7.4 cc	N <sub>2</sub> at 27° and 706 mm.
		Found		Theory for C <sub>21</sub> H <sub>21</sub> NO <sub>2</sub>
Nitrogen	I.	4.77 p. c.		4.39 p. c.
	II.	4.48 "		
	III.	4.30 "		

*Application to Carvacrol.*—2.05 g. phenol and 1.55 g. isocyanate were dissolved in 15 cc petroleum and heated exactly as for thymol with much the same results, except that after the last heating only a faint covering of crystals on the wall appeared. By cooling in a freezing mixture 1.05 g. of the crystals were recovered. After long standing the reaction mixture had only a thin covering on its walls. The yield is 35.9 p. c. on isocyanate used. The melting point of the original crystals was 114°. The first crop from alcohol melted at 117° to a turbid liquid, while the second crop obtained on dilution melted to clear liquid at 119°. It forms fine separate needles and felted masses.

Neuberg and Hirschberg<sup>17</sup> claim to have obtained a yield of 43 per cent. of a reaction product by heating carvacrol and the isocyanate together and allowing them to react. It was separated from the by-product di- $\alpha$ -naphthyl urea by filtration of the acetone solution. They obtained needles melting at 287-288°, when heated rapidly. The substance analyses correctly for nitrogen content as they found 4.82 p. c.; while the calculated is 4.39 p. c.. Their product decomposed on slow heating and even on keeping. The melting point of di- $\alpha$ -naphthyl urea was found to be 264°. In working up the slightly soluble portion of the reaction mixture from hydrothymoquinone, crystals were obtained melting at 266-270°, which were very likely the urea as they appeared also in the reagent itself when exposed to air, and melted at 264° from alcohol.

Analysis by the Kjeldahl method, using copper sulphate, gave results that were too high:

Analysis by Dumas' method gave value as recorded.

I.	0.2016 g.	gave	8.2 cc	N <sub>2</sub> at 26° and 708 mm.
		Found		Calculated for C <sub>21</sub> H <sub>21</sub> NO <sub>2</sub>
Nitrogen	I.	4.36 p. c.		4.39 p. c.

<sup>17</sup> Neuberg and Hirschberg, *Biochem. Zeit.*, 27 (1910), p. 343.

It thus becomes apparent that the substance which Neuberg and Hirschberg had obtained was not the  $\alpha$ -naphthyl urethane of carvacrol but a decomposition product of  $\alpha$ -naphthyl isocyanate or a mixture which happened to yield a result for nitrogen about what they expected. The substituted urea obtained directly as a decomposition product of the isocyanate in the air melts at  $264^{\circ}$  or a little higher, the melting point of their urethane, but contains 8.98 per cent. nitrogen.

The carvacrol compound isolated here is similar to the thymol compound, perfectly stable, colorless needles or felted needles, and exactly similar to the phenyl urethane as regards these properties and soluble with practically the same characteristics. These four derivatives are strictly analogous and belong to the same type.

*Application to Hydrothymoquinone.*—By analogy with phenyl isocyanate  $\alpha$ -naphthyl isocyanate should form the diurethane. The reagents were taken in that proportion: 2.26 g. isocyanate to 1.21 g. phenol, and boiled under a reflux with 20 cc. petroleum. The crystalline product never completely dissolved showing that some reaction took place on mixing the reagents. During heating a mixture of partially melted crystals deposited. This behavior is similar to that with phenyl isocyanate. The crystalline product recovered weighed 2.288 g. corresponding to a yield of 67.8 per cent. of the diurethane based on the isocyanate taken or 93.8 per cent. of the monourethane based on the phenol taken.

When plunged into a bath at  $135^{\circ}$  the substance melted to a turbid liquid, which cleared finally at  $180^{\circ}$ . After solution in alcohol, a slightly soluble portion crystallized out on cooling. This melted at  $266-270^{\circ}$  and corresponds to the urea obtained as a by-product.

In other particulars this reaction product revealed itself to be a mixture. Alcohol separated a slight amount of a crystalline product sufficient for an analysis and melting point. Its behavior toward solvents suggested a monoderivative. It formed white microscopic crystals from alcohol, melting at  $147-148^{\circ}$ , with softening at about  $142^{\circ}$ . Analysis gave the following:

I. 0.1343 g. gave 5.6 cc  $N_2$  at  $24^{\circ}$  and 768 mm.

	Found	Calculated for $C_{21}H_{21}NO_3$
Nitrogen I.	4.50 p. c.	4.18 p. c.



An hydroxyl group is present because it dissolves in 5 per cent. sodium hydroxide with a slight color, and this deepens on standing or boiling. When carefully neutralized with hydrochloric acid it is precipitated out again.

The residue which melted at  $266-270^{\circ}$  was small in quantity and was known to be mixed with the urea derivative; so it is not known whether the diurethane forms under these conditions, or in what proportion it may be present.

*Application to Hydrothymoquinone Dimethyl Ether.*—The ether (2.0 g.) and phenyl isocyanate (2.4 g.) were boiled with 20 cc. of petroleum under a reflux for an hour. On cooling a few crystals appeared which were probably diphenyl urea. It was boiled another hour and nothing came out.

Leuckart<sup>17a</sup> discovered that thymol methyl ether reacts with phenyl isocyanate in the presence of aluminum chloride. The resulting product is methylisopropyl methoxyl benzanilide.

Accordingly this reagent was added to the reaction mixture. Warming to boiling initiates a spontaneous reaction, which keeps the mixture in gentle ebullition for a few minutes. The color did not change, but on heating crystals began to appear and a liquid distilled into the condenser which returned to the flask in drops, causing sputtering.

The product was filtered from the petroleum, decomposed with cold dilute hydrochloric acid and taken up in alcohol, in which it is as readily soluble and as easily recovered as the monourethanes. The color was discharged by boiling with bone black. After crystallization once from alcohol 1.5 g. were recovered. It melted at  $240-241^{\circ}$ . Re-crystallized, it melted at  $240-241^{\circ}$ , and treated with boneblack at  $240^{\circ}$  exactly. The crystals are white, appear as radiating clusters of needles and resemble, in solubility also, the monourethanes of thymol and carvacrol.

Upon digestion in sulphuric acid, it gave an oil which steam distilled at first but dissolved and cleared up completely in one and one-half hours.

I. 0.2984 g. required 29.11 cc N/10 HCl.  
 II. 0.3108 g. required 30.20 cc N/10 HCl.

	Found
Nitrogen	I. 13.67 p. c.
	II. 13.65 p. c.

<sup>17a</sup> Leuckart, J. pr. Chemie, II, p. 320.

The Dumas method gave results very close to these on material dried at 130° for one hour.

I. 0.1432 g. gave 19.6 cc N<sub>2</sub> at 22° and 705 mm.

	Found
Nitrogen	14.8 p. c.

A methoxyl determination gave no turbidity in the silver nitrate solution after four hours; so there cannot be methoxyl groups present. This percentage of nitrogen does not correspond with any possible arrangement of the nuclei, because the isocyanate itself has only 11.77 per cent. nitrogen.

#### DIBENZOYL HYDROTHYMOQUINONE

The reaction by which this formed is the ordinary Schotten-Baumann reaction in which the phenol was dissolved in the theoretical quantity of 15 per cent. sodium hydroxide and a sufficient quantity of benzoyl chloride added to leave an odor at the end.

Five grams of hydrothymoquinone (3 mols) were dissolved in a slight excess (20 cc.) of 15 per cent. sodium hydroxide. To the brownish solution 8.4 g. of benzoyl chloride (6 mols) were added and the mixture shaken. Heat was evolved and a pale yellow, crystalline solid separated. The filtrate yielded some benzoic acid on acidification, but this may have been derived from the excess of alkali. The moist solid was washed at the pump and treated with about 40 cc. of 95 per cent. alcohol and boiled. A solution resulted, orange-yellow in color, which deposited crystals on cooling. These were taken up in alcohol and the undissolved portion from the first treatment also dissolved in this solution.

The crystals appeared as coarse needles, very slightly yellowish or as a finely granular white powder.

From dilute alcohol (1st)	1.16 g. mp. 138-140°.
From 95 p. c. alcohol (2nd)	4.74 g. mp. 141-142°.
From 95 p. c. alcohol (3rd)	2.59 g. mp. 141-142°.
Yield	<hr/> 8.49 g.

On the basis of the dibenzoate, C<sub>10</sub>H<sub>12</sub>(OCOC<sub>6</sub>H<sub>5</sub>)<sub>2</sub>, this represents a 75.5 per cent. yield, as computed only on that recovered from the alcohol by crystallization. On analysis:

0.2374 g. gave 0.6760 g. CO<sub>2</sub> and 0.1346 g. H<sub>2</sub>O

	Found	Theory for C <sub>24</sub> H <sub>22</sub> O <sub>4</sub>
C	77.7 p. c.	76.96 p. c.
H	6.3 "	5.93 "

Its melting point is very close to that of the original hydrothymoquinone; so tests were made to establish its identity. The hydroquinone dissolves slowly in 5 per cent. sodium hydroxide with a red-brown color. The dibenzoate was unacted upon during the same time. With a little thymoquinone, the hydroquinone in alcohol evaporated leaving a purple film and purple crystals. The dibenzoate evaporated, leaving yellow crystals of unchanged quinone, but no quinhydrone color at all. Finally a mixture of the two was melted along with the constituents on the same thermometer:

Hydrothymoquinone .....	mp. 144-145°
Dibenzoate .....	mp. 143-144°
Mixture .....	mp. 123-125°

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## INDIRECT SERVICES OF PHARMACY AND PHARMACISTS.\*

BY E. G. EBERLE, PH.M.

PHILADELPHIA, PA.

This title has been chosen, not because it fits the paper throughout, but because a number of the references in it relate to such services. I hope you will not expect my feeble effort to entertain; it may not even present a formidable thought that can be applied with profit, and perhaps the brevity of the paper will please you most. However, there is a reason for the presentation, which has been prepared in response to a request by Dean LaWall, to say something on the occasion of a monthly Faculty meeting, and came just after looking over the report of the Convention of the American Pharmaceutical Association in New Orleans, in 1891. It impressed me with the indirect services rendered by pharmacy and pharmacists, and that which has been stated in many ways:—we receive by giving, and in real service both the giver and recipients share. In this way

\*Read at the monthly meeting of the Faculty of the Philadelphia College of Pharmacy and Science.

the common fund of knowledge is created and we draw on this heritage while giving something thereto for others. Macaulay has stated this succinctly: "Every generation enjoys the use of a vast hoard bequeathed to it by antiquity, and transmits that hoard, augmented by fresh acquisitions, to future ages." That is one of the points it is endeavored to bring out in this paper.

You assemble at these monthly meetings to exchange views on various subjects, to communicate the results of your observations, of comparing these and then to combine them or abstract from them for your profit and that of others. Your own worth is greater by observing the reception of your teachings and the application of them by the students, and their knowledge is more firmly fixed when observation accompanies their study and work.

The complexity or diversity of knowledge is illustrated in modern pharmacy—pharmacy is a science and an art, and as conducted in the United States, and almost every other country for that matter, is a business and profession. Quite naturally the American Pharmaceutical Association, which considers related matter in the programs of the annual meetings, is a representative organization of pharmacy, though some would have us think otherwise. There is an inter-relation of our work and investigations that have part in many lines of research. There is a branching from subjects that interest us into many industrial problems and promotions; some are of more importance to us, while others find far wider application elsewhere. That Herman Frasch worked in the laboratories of the Philadelphia College of Pharmacy under Professor John M. Maisch has its significance; the results of his later work concerned the world. Scheele's discoveries, while primarily for pharmacy, had a large part in the development of the chemical industries. When we think of Pasteur, his aid to medical and surgical practice impresses us, along with his achievements for silk culture, preservation of the grape culture of France, and industries in which knowledge of fermentation is greatly concerned.

When we study the system of training and education begun nearly one hundred years ago in the Philadelphia College of Pharmacy, we are made aware that this institution can be credited, in part, with the plan of vocational education in public schools, which the director of practical arts and vocational education in public

schools of Philadelphia said has been revolutionized in the last fifteen years. These are the words of Director Ash:

"Where formerly the pupil went out from the school poorly equipped to make any real headway for some time in his chosen vocation, if he had one, and was forced to struggle along uninformed and unguided, he now goes out, as it were, with a flying start.

"With the present system, the high school student, in the fourth year of his chosen course, spends two weeks out of every school month in an industrial establishment, actually working and producing, and earning a good salary.

"In 1906 the vocational idea got a real foothold in the schools, and the amazing growth of this feature, both in interest of the pupils and effectiveness in the teaching, is now a matter of history."

The Philadelphia College of Apothecaries adopted the idea one hundred years ago and has successfully applied it in the system of teaching. It has aided thereby in the development of many industries. The apprentice system has practically disappeared, but the idea put into practice by these apothecaries in 1821, to co-ordinate education and training, remains and has been fitted and shaped into the scheme of the high schools a plan that has the advantages pointed out by Mr. Ash. You will reflect on the different Philadelphia industries, more or less closely connected with pharmacy, in the development of which P. C. P. graduates had a direct or indirect part.

It has been truly said that the problem of education is much larger than the individual and his trade or profession, it is as big as society itself; the work of a profession, an institution, an organization, is measured not only by the results of and for those directly concerned but also by the influence on society or the world at large. Pharmacists have been more or less derelict in informing the public relative to their part in the world's work; the credit in which they should have shared has gone to others. Their work in associations is often belittled by their own number and not infrequently hindered and impeded, if the results are not absolutely neutralized or passed to the credit of others who are only too willing to utilize what has been done by pharmacists. Physicians link up their service with the life of citizens; chemists advertise their achievements, their value to the industries and commerce, while the contributions of pharmacy in that respect are often ignored and the credit then goes to others, because we do not contend for rightful

recognition, nor place sufficient value on our accomplishments and achievements.

Commerce of the past and present has been largely developed due to the search for drugs; the materia medica has been improved, and gives physicians assurance of results by undervalued—to some extent uncredited—study and investigations of pharmacists. Only recently a place was given in New York University Hall of Fame to another for the discovery of ether as an anesthetic that should have been accorded to the physician-pharmacist, Dr. Crawford W. Long. The research work of Dr. Edward Kremers and co-laborers has great possibilities; the investigations of Professor J. U. Lloyd have received rightful recognition and place in colloidal chemistry, but the record should be kept straight. An exploration in the interest of science has been made possible by H. K. Mulford Company, under the direction of Dr. H. H. Rusby, who has heretofore searched the wilds of South America, and with the purpose of serving humanity.

All of these preliminary references—many of them of very much greater import than the subject I have chosen—have the purpose of bringing in the main topic of the paper in which some of the connections of pharmacy with the industries are shown, and incidentally to point out wherein some of the annual meetings of the American Pharmaceutical Association afford opportunities for papers that will extend our knowledge and usefulness to the world. The thought is not new, but sometimes the opportunities for applying it are overlooked.

The paper referred to was presented by Charles Mohr, for about thirty years a member of the American Pharmaceutical Association, now deceased, a friend and correspondent of the late Professor John M. Maisch, on *Vegetation of Louisiana and Adjoining States*. The blending in this section of the country of southern and northern vegetation is sufficient inference that a large number and variety of plants were considered in his paper, comparatively few of them are of great medicinal importance, the greater portion dealt with the pines, in which the author was particularly interested, being employed by the United States Government to secure all available information thereto. He went somewhat into details of collection and yield of the turpentine, and also the manufacture of sugar from cane. Items of lesser importance were the citrus fruits, cam-

phor and fibre-producing plants. The interest of pharmacy in the more important items of the paper are relatively small, but the industries are largely concerned. Just now the high price of paper affects the cost of the Association's publication, and hence the discussions on the value of the pines for paper pulp attracted my attention; also the connection of pharmacists with this industry; further, the fact that as a new source of paper pulp cotton-stalks are now being utilized, and several pharmacists have been among the first to suggest the use of them for that purpose, and are preparing to manufacture from that source. Deductions of the discussions also are applicable to some of my preliminary statements, as will be seen. It was brought out that loblolly pine was suitable for making paper pulp, also the cotton-wood, and Joseph P. Barnum, member of the American Pharmaceutical Association, from Louisville, Ky., then interested in the manufacture from these sources, informed the members that a young lady, a graduate in pharmacy, had charge of their factory in Louisville.

The concluding remarks of Mr. Mohr evidence what has been stated, namely, that the one who contributes information profits, when he said in substance, that he was glad to have this information, of which he was entirely ignorant, being charged with the duty of bringing before the Government all that pertains to the pines, for the purpose of utilizing the wood to the greatest economical advantage, in fact all that relates to these woods; he thanked the members for the information he had received from them. It will be admitted that such papers increase the sum of our knowledge and add to our powers of direct usefulness, and may benefit the section of the country wherein the meeting of the Association is held.

The sources of paper pulp have been better developed elsewhere, and only in a limited way in the South; however, within the last month northern financiers have decided to increase the capacities of the paper pulp mills of the Great Southern Lumber Company, located in the section where this discussion before the American Pharmaceutical Association took place. And, what is equally or more interesting, it is proposed to plant loblolly pine on cut-over lands, this wood growing to cutable size in fifteen years for wood paper pulp, so that by the time the standing timber is exhausted the new forest will be of good size. Immediate plans provide for an investment of eight million dollars, according to newspaper reports.

Another subject considered in Mr. Mohr's paper related to the manufacture of cane sugar. Recently manufacturers of products in which sugar is largely used have invested in sugar lands, with the purpose of raising cane and manufacturing sugar. A well-known Philadelphia pharmacist, Josiah C. Peacock, now engaged in other work, has been active along these lines.

The life and activities of Charles Mohr have a bearing on the title of this paper exemplifying by the work of one pharmacist the indirect services of pharmacy to industry and by his investigation added to the source of our knowledge. Therefore a running sketch is deemed of interest.

Charles Mohr was born in Germany in 1824. His father was engaged in chemical manufacturing, and several of his relatives were in one way or another associated with the Forestry Divisions. At the age of twenty-one he made his first exploring trip, which was to Northern South America in 1846, from whence, after a short stay, illness compelled his return home. In 1848 he came back to the United States, visited New York and Philadelphia, and thence went West, locating for a time in Cincinnati, where he became associated with a German manufacturer of chemicals. In 1849 he joined a party going to California, and on this journey lost his herbarium; and soon after coming to the mines was taken sick, and travelled on to San Francisco. In the meantime he had again made quite a large collection of plants.

He concluded to go to Panama. Soon after he arrived there he was attacked with fever and decided to return to the United States. While sick, his collection of plants was stolen. In December of 1850 he came back to Cincinnati, and from here settled on a farm in Clark County, Indiana. Farm labor not agreeing with him, he removed to Louisville and became assistant to an apothecary, in which firm he soon thereafter became a member. He then renewed his botanical studies with Leo Lesquereaux, taking up the mosses, which work was not published until in 1884.

On account of the condition of his health he travelled South to Louisiana, and thereafter to Vera Cruz, where he landed in the early part of 1857. There he engaged in pharmaceutical business, but on account of a revolution he was compelled to leave and returned to the United States, landing in Mobile, December 1857, and soon en-



gaged in the drug business there; this was continued until 1892, when he turned this business over to his son.

In 1860 he studied the ferns, and this work was published in Eaton's *Ferns of North America*. When the war between the States broke out he manufactured drugs from native resources. After the war, during the reconstruction period, he studied the fertilizing value of the ashes of various woods, and lectured throughout Alabama and wrote articles on this subject, in order to aid in the improvement of exhausted soils and betterment of agricultural practice.

In 1876 he was appointed to investigate the gold and other mineral resources of Alabama, which took him through all parts of the State and gave him the opportunity of studying the flora, which observations were published in Berney's *Handbook of Alabama* in 1878, under the title of "The Forests of Alabama and Their Products" and *The Grasses and Other Forage Plants of Alabama*. The value of his collection of minerals is shown by the fact that they were exhibited at the exhibition in Mobile in 1876, and also in Atlanta in 1881.

In 1887 he reported for the United States Department of Agriculture on the Economic Geology of Alabama. His treatise on Grasses and Forage Plants of Alabama was prepared for the United States Department of Agriculture in 1878 and 1879, and was also published in the *Botanical Gazette* for May, 1878, wherein he gave an account of the useful plants of foreign origin which were acclimated in the Gulf States. In 1878 he also began to arrange his herbarium of Alabama and prepare a preliminary list of plants growing there without cultivation. This was included in the Geological Survey of 1890, and later the plant life of Alabama was published.

In 1880 he was appointed to collect information for the Tenth Census Report on the Forestry Conditions in the Gulf States, and during this time he also collected for the Harvard Arboretum and for the Jessup Collection of the American Museum of Natural History. The latter was published in book form—*The Forest and Timber Trees of Alabama*. In 1882 he arranged the agricultural and forestry collection for the Department of Agriculture.

In 1883 and 1884 he was employed by the Louisville & Nashville Railroad to study the agricultural, forest and mineral resources along the line of its road. He also reported on soil and climate in

this territory. The collections made were placed on exhibition in New Orleans in 1884, and also at the Louisville Exposition, and a descriptive catalogue was published, under the title of "The Natural Resources of Alabama."

In 1892, as previously mentioned, he turned over the drug business in Mobile to his son, and devoted his time to plant life of Alabama and in the investigation of the flora of North America for the Division of Forestry, United States Department of Agriculture, and in arranging his herbarium of the plants of Alabama for the State University. A set of these plants is displayed in 150 glass front cases, showing the foliage, flowers and fruit of the forest trees, and the herbarium is known by his name.

His work on the pines was published in 1896, and then followed his monographs on the cypress, the juniper and red cedar. Monographs of the hard woods were to be published next, but he had just completed that on the oaks when he died in 1901.

In 1900, he moved to Asheville, N. C., where he spent most of his time in the preparation of the monographs mentioned. He completed *The Plant Life of Alabama*, but did not live to see the finished book, which came from the press a week or two after his demise. He was also preparing *The Economic Botany of Alabama*, in which were to be given full accounts of the useful and noxious plants of the State. This was to be the crowning work of his life. The Biltmore Herbarium and forests afforded him the opportunities for his studies. Here his last illness overtook him. Though suffering greatly for a number of days preceding his death, the last words he spoke, to be understood, were, "How beautiful the world is!"

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## PHARMACEUTICAL RESEARCH.\*

BY GEORGE M. BERINGER, A.M., PH.M.

The most ancient records available show that from time immemorial the progressive peoples of each period recognized that the preparation and dispensing of medicines was an important vocation to be entrusted only to those specially trained and educated to perform such duty to society. In ancient Egypt the priests of Isis alone

\*Address delivered before the New York Branch of the American Pharmaceutical Association, January 10, 1921.

compounded and dispensed the prescriptions of the physician priests. The Israelites evidently held the apothecaries in high esteem, as the Biblical records contain a number of references to them and their work. The holy anointing oil and the incense were both directed to be "compounded after the art of the apothecary." To Eleazar of the priesthood, the son of Aaron, was entrusted the services and duties at that time performed by the apothecary. So we as pharmacists can take just pride in that we are engaged in a most ancient and honored calling.

The student of the history of pharmacy is soon brought to realize that pharmacy has played no small part in the world's progress and that pharmacists have made many valuable contributions to the knowledge of materia medica, botany, chemistry and the allied sciences, and that some of these, of the greatest benefit to mankind, are constantly employed in the professions and industries. He likewise becomes painfully aware of the fact that oftentimes the credit is given to, or taken by, other branches of science. The writers of Encyclopædia articles and similar works of reference are specially faulty in their failure to recognize the importance of the contributions of the unobtrusive workers in science despite the services of incalculable value that these have rendered to mankind. To most of these authors and compilers the activities of the warrior, the statesman, or politician, so often destructive of the world's progress, and even of the novelist seem to be of paramount importance for perpetuation. Since the influence of pharmacy has been quite commonly overlooked by these general historians, it remains as one of the duties of pharmacists to see that the scattered data and facts concerning the lives and contributions of pharmacists are collected, preserved and published, so that it shall be established beyond peradventure as to whom credit is justly due.

Throughout the medieval period, and especially that portion which is referred to as the age of the alchemist, the contributions to the sciences were largely made by the investigators in medicine and the apothecaries who were aiming to improve the methods of preparing their remedies and of discovering new substances of therapeutic value.

Among the English-speaking nations there has been unfortunately a too apparent disposition to disparage the work of the apothecaries, and during the Fourteenth Century they were commonly re-

ferred to as the "physician's cook," and even in comparatively recent times, as the "physician's handmaids." It is apparent to the student of history that a relatively small percentage of medical practitioners have been engaged in actual research work, and that a goodly number of pharmacists have carried on research in behalf of pharmacy that will compare favorably with any that has emanated from the medical branch.

I cannot at this time delve too deeply into the debt of the world to pharmacy, for I conceive that a discussion of that topic would occupy the entire evening and preclude the consideration of the subject that has been assigned for this time. Nevertheless, it has such a close association with the subject of research that I cannot refrain from giving a few illustrations that must serve the purpose of the present occasion.

The study of the sciences undertaken by Davy as an apprentice to a surgeon-apothecary no doubt gave him his first insight into chemistry and determined the bent of his mind toward chemical research. The results of these investigations won for him reward and undying fame as the discoverer of a number of the important chemical elements.

That peerless indefatigable experimenter and ideal research worker, Karl Wilhelm Scheele, is constantly referred to as the great Swedish chemist, and his name is scarcely ever associated with pharmacy. Yet he studied pharmacy, and for the major part of his comparatively short life depended upon this calling for his livelihood. During the last eleven years of his life, he owned and managed a pharmacy, and was supported thereby while carrying on some of his most successful experiments. His activities and investigations cover a very wide range of topics of the utmost importance to mankind. The discoveries of Chlorine, Barium, Manganese and the investigations of its applications to the glass industry, of Tartaric Acid, Arseniuretted Hydrogen, his studies of the cyanides such as Prussian Blue and Hydrocyanic Acid, and of the composition of the atmosphere are but some of the contributions of this pharmacist to the world's progress. These can be traced largely to the contact with the wares and the problems of his chosen vocation. Who is prepared to estimate the world's indebtedness to this studious, observing and painstaking worker, many of whose discoveries are still in daily application in our industries?

Klaproth is another apothecary whose early investigations of the composition of pitchblende led him to the discovery of Uranium, and this was the initial step that has led up to the discovery of that remarkable group, the radio-active elements.

In the field of organic chemistry important contributions to our knowledge can be traced to pharmacists, and numerous are the illustrations available. I must here content myself with only citing for your attention the fundamental work of Sertürner, and of Pelletier and Caventou upon the alkaloids. The galaxy of brilliant investigations emanating from pharmacists who have engaged in research in this interesting domain covers nearly every civilized nation, and these have been of inestimable value in the practice of medicine.

Research is best defined as a careful search for the truth, and so it can be safely asserted that no authoritative work is accomplished, no scientific investigation or discovery is made, and no theory that is sound is propounded that is not based upon research.

Research is generally subdivided into that which is "pure" and that which is "applied." The distinction is made upon the basis of the latter being undertaken with a specific need in view and that the results will be applicable to the solving of some industrial and commercial problem usually of monetary advantage. Practical application is commonly the reason that actuates the establishing of research departments in most of our large industries. No one can take exception to this, as eventually the discoveries and inventions made are disseminated to the advantage of all. Yet there is a feeling held by the real scientists that personal interest should not blind one to the obligation of true citizenship, to contribute his full share toward public welfare and scientific progress.

Although the truly scientific and enthusiastic research worker engages in "pure research," possibly with the thought of clearing up some abstruse question that, while advancing our sum of human knowledge, may at the time have no apparent practical application, it happens oftentimes that his work and discoveries become of exceedingly great value and unexpected important application. The discoverer of the Hertzian waves had no thought of the utilitarian value of his discovery and the later application thereof to wireless telegraphy. The investigation of our own Professor John Uri Lloyd on the subject of precipitates in fluidextracts was undertaken because the question was deemed a pharmaceutical problem of the time demand-

ing attention, and his publications were then considered simply from a pharmaceutical viewpoint. We are now proud of the association and the distinction awarded these by Dr. Wolfgang Ostwald as fundamental and important early studies in colloidal chemistry and to claim the credit for priority of publication in the proceedings in the American Pharmaceutical Association.

Recently we had the pleasure of listening to a lecture by Professor Edward Kremers, of the University of Wisconsin, in which he detailed the investigation carried on for upwards of twenty-five years on certain American species of *Monarda*. His studies of the aromatic principles and the other constituents of these plants, constitute an elaborate piece of pharmaceutical research that is destined to become a classic contribution to phyto-chemistry. While it may now be viewed as a pure scientific investigation, whose main value will be as a pioneer and in its suggestion for similar investigations directed to other groups of plants, it has cleared up a number of points relating to the source, composition and production of some of the important aromatic plant constituents, and I predict that it will prove of material assistance and pecuniary value to the industries engaged in preparing these on a commercial scale.

The history of *Cinchona* cultivation is an interesting narrative of scientific research applied to every phase of the subject. The selection of the species and varieties of *Cinchona* yielding alkaloids; the study of the alkaloidal content of the different barks; the problems of soil, climate, and altitude and their influence upon the character and percentage of alkaloidal content of the bark; the production of varieties yielding the largest percentage of Quinine; the study of the localization of the alkaloids in different parts of the plant, the effect of climate, season, etc., upon these and their transformation from amorphous to the crystalline state during the development of the plant organs; the discovery of the value of partial stripping, the best time for this operation, and the renewal of the bark by mossing; the modern methods of marketing the bark and alkaloids; the improved process of manufacturing the alkaloids in a high degree of purity; these are some of the problems that had to be worked out scientifically, and the value of the results from either a commercial or a humanitarian viewpoint is beyond calculation. It is a gigantic example of practical applied scientific researches. Notwithstanding all that has been accomplished by the study and scien-

tific investigation of the Cinchonas, the subject is not exhausted. The paper by Howard and Chick on "Some Recent Samples of Grey Cinchona Bark,"<sup>1</sup> demonstrates the necessity for a thorough re-investigation of the grey cinchonas of Peru to determine positively, by newly collected authentic specimens, the species yielding the bark containing the high percentage of cinchonine reported, and whether this was due to the altitude at which the trees grew. This paper presents the possibilities for duplicating the cultivation of the Ledgeriana variety of Cinchona Calisaya in which quinine almost alone is present to a high percentage by the cultivation of a selected Cinchona of the grey bark group for the production of cinchonine.

In addition to the classification of research as "pure" and "applied," I would advocate a further subdivision as especially applicable to pharmacy; namely, major and minor investigation in both pure and applied research. Every apothecary has opportunities from time to time to note improvements in formulas, methods of manipulation and niceties in compounding, what our friend Thomas McElhenie calls "wrinkles." These observations, although they may appear individually as comparatively insignificant, yet, if they be but suggestions for improvement, in the aggregate they will make toward a substantial advancement in the art of pharmacy. As a part of his collegiate training and to inculcate the faculty of observation and deduction, every student in pharmacy should have assigned, some topic of pharmaceutic interest for special study, investigation and report, even though these subjects be but very elementary problems in pharmaceutic research.

Notable events have marked influence in stimulating the character of research and the results achieved. The foundation of a school of pharmacy in America for the systematic education of pharmacists had a decisive effect in the development of such characters as Daniel B. Smith and Dr. George B. Wood, and this event was the stimulus to which may be attributed the preparation of that master work the *United States Dispensatory*.

The introduction of the process of displacement made the subject of percolation and the preparation of the various classes of galenicals by this method, topics demanding extensive experimentation, and as a result we have recorded the classical investigations

<sup>1</sup> *The Pharmaceutical Journal and Pharmacist*, July 24, 1920. Reprinted in *THE AMERICAN JOURNAL OF PHARMACY*, October, 1920.

of Procter, Squibb, Diehl, Lloyd and others as contributions of great practical worth to pharmacy.

The events of the Civil War presented new opportunities for pharmaceutical research and the further development of such pharmacists as Maisch and Squibb. The Southern States were compelled to rely much upon their natural resources. To meet this necessity Dr. Francis P. Porcher wrote his book on *The Resources of the Southern Fields and Forests, Medical, Economical and Agricultural*, and this work is still frequently referred to as an authority.

Dr. Charles Mohr, a southern pharmacist, likewise, made many valuable scientific investigations of the natural products and resources of several of the Southern States and his contributions to our literature are of great practical value to medicine and pharmacy as well as to botany.

The organizers of the American Pharmaceutical Association in 1852, had in mind as main purposes, the improvement of the quality of drugs imported and the better education and protection of pharmacists. The objects announced suggested research, and this organization has ever since been the nucleus around which has been gathered the principal research workers in pharmacy, and its publications have been the mediums for disseminating the far-reaching results.

The great World War forcefully demonstrated the necessity for co-ordinated scientific research, applicable to the industries as well as to modern warfare. As a war measure, the National Research Council was organized in 1916 primarily for the purpose of stimulating and co-ordinating research on war problems. In 1918, by executive order of the President of the United States, this was re-organized as a permanent body, and the announcement was officially made that "its essential purpose is the promotion of scientific research and of the application and dissemination of scientific knowledge for the benefit of the national strength and well being." It is now chartered as the National Academy of Science. Despite the far-reaching possibilities and effects of pharmaceutical research and the importance to mankind of a thorough knowledge of all remedial substances, and that pharmacists are the logical persons for the carrying on of such investigations, it remains a fact that so far pharmacy has not been recognized in the plans of the National Research Council, and that there is no evidence that pharmaceutical research is to be given any encouragement.



The thorough study of the numerous medicinal products supplied by pharmacists, and the processes employed in securing and preparing medicines will open up boundless fields for study with innumerable research problems, the possibilities of which and the value thereof to mankind cannot be estimated. Suffice it to proclaim that "the sum of scientific knowledge for the benefit of the national strength and well being" acquired thereby, will hold no secondary place.

The practical issue at this time and an important question before American pharmacists is how pharmaceutical research can be systematized and organized so that the importance of co-operation of this branch of scientific investigation will be fully recognized, and an appropriate place in the scheme of the National Research Council be assigned to pharmacy.

The field open to pharmaceutical research is now not more restricted than formerly, but on the contrary, is continually expanding and it is but a fair inference to assert that the value of the past investigations can be more than duplicated by those of the future. There is no lack of opportunity for pharmacists to engage in study and research, and the present generation should not let the imputation rest that there is now less desire. An observing writer has recently stated that pharmacy has never been more in need of research upon strictly pharmaceutical problems than at the present time.

There is scarcely a topic associated with the practice of pharmacy on which the available knowledge can be said to be complete. Innumerable are the questions requiring further study arising from the natural kingdoms and all quarters of the globe from which medicines are obtained. The methods and processes employed in pharmacy are not yet sufficiently understood, and despite all the work done on percolation, and all that has been written thereon, the last word has not yet been spoken. The value of the various solvents and their appropriate use in the extraction of different drugs is still an open question, meriting further extensive investigations involving in each drug a study of its active constituents and their behavior to solvents "in situ" and after extraction. The revisions of our national standards, the Pharmacopœia and National Formulary, call for continuous research along many lines. The tests and assay processes are constantly undergoing revision and must be considered on the whole as tentative and requiring much further

review and improvement. The botanical source of some of the official vegetable drugs is still undetermined, even though these may have been in use for many generations. The proper time for collection of vegetable drugs and the approved methods for their preservation, drug plant cultivation, the effect of soil, climatic conditions, altitude, etc., the percentage of active constituents and the study of the localization of these in the respective plants remain fertile fields for study. The voluminous and excellent work of such men as Tschirch, Oesterle, Moeller, Dragendorff, Flückiger, Koch, Zörnig, Hanbury, Holmes, Greenish, Collin, Maisch, Kraemer, Bastin and Trimble in developing the knowledge of pharmacognosy and plant chemistry, but serves to demonstrate the vastness of the field yet unexplored. The enzymes; the ferments; the vitamins; the animal organ drugs, such as the endocrine gland products; the synthetic chemicals; as well as the new remedies that are being continually introduced into medical practice, present an endless variety of topics demanding the attention and investigation of pharmacists. The text-books, and even the legally recognized official standards contain statements that are in need of verification and it is an imperative duty that these be critically examined and that each erroneous or misleading statement be either corrected or eliminated.

In citing these various lines of research open to pharmacy, it must be understood that I have offered these merely as examples and not as an enumeration of the extensive field of exploration available for the application of systematic pharmaceutical research.

The need is that pharmacists themselves, as well as scientists engaged in other fields of research, should have a correct view of the possibilities and the comprehensiveness of pharmaceutical research. The investigations properly coming under this classification have many points of contact with other fields of research, and herein is the need for co-ordination and co-operation, and the reason why pharmacy should be properly represented in any plans for national scientific research. The problems arising in the laboratory of the manufacturing pharmacist are, of course, important and should receive searching study and investigation, but not from a selfish standpoint alone. His problems can best be solved by co-operation not only with his fellow manufacturers, but by that of research workers in the sciences involved in the questions at issue, and the benefits of such research belong to "the national strength

and well being." However, to limit the pharmaceutical research to such a narrow field would be to have it serve only the selfish end of a few.

Many of the problems arising in pharmacy are of a chemical nature, but to limit pharmaceutical research to chemical problems would be a very narrow construction. Likewise, it is important that the pharmacologic action of synthetic remedies should be carefully studied and their therapeutic value accurately defined, but to limit the field of pharmaceutical research to such pharmacological investigation, as was at one time proposed, evidences a lack of conception of true pharmaceutical research and its proper scope. True, all of these and many more lines of scientific investigation are points of contact and co-operation of pharmacists with other research workers. Pharmaceutical research cannot, however, be classified with medicine, nor with chemistry or with any of the other lines of research so far recognized. Pharmacy performs a distinct duty to the public and should be accorded recognition as a distinct vocation with problems of national interest and welfare peculiar to its field of service. All of the propositions for pharmaceutical research that have so far emanated from those outside of pharmacy have only demonstrated the insufficiency of the view, and a failure to comprehend the extensive fields awaiting organized pharmaceutical research.

Pharmacists must themselves, have a proper conception of the present and a broad vision of the future possibilities. The salvation of pharmacy and its establishment upon a solid basis as a profession founded upon scientific studies and investigation, rests entirely upon the pharmacists themselves. The investigations of the past have been largely carried on by the individual workers engaged as teachers in the schools of pharmacy, or as experts in the laboratories of the manufacturers, and by a few retail pharmacists. There has been no systematic attempt to co-ordinate pharmaceutical research or make it a co-operative division of a national comprehensive research plan. Pharmacy has been like an ocean-going steamer with good engines and a compass, but no navigator.

We must now realize the changed condition of the times resulting partly from the war necessities, and partly from the advanced position assumed by those who have been placed in charge of the National Research Council. This organization is composed of

those associations or societies that have as a basis for membership research. Consequently, if pharmacy would seek a part in the scheme of this co-operative national movement, it must organize its research committee, association or section composed of research workers and those interests in pharmacy that are concerned in research, so that scientific pharmaceutical investigation will be stimulated and properly directed.

It would appear that the American Pharmaceutical Association is the proper body to organize pharmaceutical research that it may be assigned to its proper field of usefulness and correlated in the scheme of the National Research Council, and its Committee on Research is charged with this duty. The American Pharmaceutical Association is acknowledged to be the scientific support of the drug industries and the organization of research must now become another means of exhibiting its leadership and useful activity in behalf of pharmacy. It must hold aloft the torch of learning and transmit the knowledge acquired from the contributions of the past with increased brightness and added store and energy to the future generations.

Upon the Colleges of Pharmacy we must rely for support. Not only should their faculties be composed of enthusiastic research workers capable of carrying on scientific investigation, but every student in the higher or post-graduate courses should be given training in the original investigations of problems pharmaceutical. This is a feasible plan by which the work of the past can be perpetuated and the needed army of research workers in pharmacy may be gradually built up of the proper material.

In closing permit me to refer to the Biological Exploration of the Amazon Basin under Dr. H. H. Rusby. While the newspapers have very commonly spoken of this as an expedition of chemists, it is organized, controlled and financed by pharmacists, and to a very large degree it is a pharmaceutical research expedition, and is typical of many more extensive pieces of research that would become feasible under an organized pharmaceutical research endowment.

## ABSTRACTED AND REPRINTED ARTICLES

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### NOTE ON THE KEEPING QUALITIES OF DRIED AND PULVERIZED VACCINE VIRUS.\*

By DR. O. SCHÖBL.

At the request of the Philippine Health Service, some experiments were made at the Bureau of Science in order to ascertain the method of preparation, and the means of preservation, of dried vaccine virus for practical purposes. The proper distribution of active virus to remote places has always been a problem in the Philippines, on account of geographical conditions, particularly in case of emergency—that is, when smallpox breaks out in a far-away place—because it takes a long time for the vaccine virus to reach its destination. Furthermore, we must take into consideration that there are localities in which there is no way of keeping the glycerinized vaccine virus at low temperature during shipment from the nearest port to these remote places.

It seems, therefore, that it is of great importance to the sanitary authorities of this country to try to distribute vaccine virus in such form that it can be kept even under unfavorable conditions; in other words, in a form in which even if direct light, and sun heat or artificial heat are excluded, the vaccine can still be kept for a reasonable length of time. Were this possible, vaccinations could be performed in the interior of islands where communication and ice plants are nonexistent. It would also benefit parts of the Islands which have both communication and ice, in as much as the health officer located in such places could keep on hand a certain amount of vaccine all the time, and if smallpox should break out in his district vaccinations could be commenced within three hours after receiving the report of the first case of the disease in the district. There are no doubt places connected with Manila, but where connection is such that, even if the health officer cable immediately for vaccine virus, several

\*Reprinted from the *Philippine Journal of Science*, July, 1920.

days, and probably a week, must elapse before the required amount can reach him.

In looking over the literature on the subject, we find very few references. Apparently in most countries which have direct communication by land the vaccine virus preserved with glycerin is satisfactory for any occasion, and no further steps need be taken for the preservation of this important biologic product. In searching for data concerning the dried pulverized vaccine, we have to go back in the literature to 1881 to find the first note on the subject. Reissner in Darmstadt, and Frappoli in Italy, appear to have been the first ones to experiment with the drying of vaccine virus. It was at that time that the preservation of vaccine virus for wide distribution and shipping was desirable; but the glycerinized vaccine virus, as introduced by Muller about the same time, became supreme, and was so satisfactory that no further attempts were made to dry the vaccine virus. As far as the Philippine Islands is concerned, we find a note on the "Preservation of vaccine virus" by E. H. Ruediger in the Bulletin of the Manila Medical Society, August, 1910.

In preparing dried vaccine naturally three requirements have to be fulfilled. First, the drying must take place as rapidly and as completely as possible, and without the application of artificial heat. Second, the preservation must be such as to keep the powder in absolutely dry condition; it must be kept away from light, particularly sunshine, and from heat. Third, the bacterial content of the dried vaccine must be considered; in the absence of glycerin, which in the glycerinized vaccine acts not only as a preservative but also as a bactericide, the bacterial content in the dried vaccine will naturally be higher than in the glycerinized vaccine.

#### EXPERIMENTS PROPER.

The vaccine was prepared in the following way: The pulp obtained by scraping a vaccinated animal was ground up in a sterile mortar, spread over a large surface under aseptic conditions and dried rapidly over a hygroscopic chemical in vacuum, ground up, perfectly dried, and kept in a desiccator at room temperature. Every week one monkey was vaccinated with a small portion of this powder and kept under observation in order to ascertain whether or not there was any difference in the development of the "take" in this monkey and that of another one, used

as control, which had been inoculated at the same time but with fresh glycerinized vaccine. Up to date of writing, that is, four months from the time the vaccine was prepared (and it was kept at room temperature all the time), we have obtained in all inoculated animals first-class "takes" which could not be distinguished from the "take" in the control animal inoculated with fresh vaccine. We cannot, therefore, at the present writing state definitely how long the dried and pulverized vaccine will keep. But, in view of the fact that the experiments showed good results during the past four months, the procedure seems to be of practical use.

In order to make the use of this vaccine as simple as possible, we have suggested that it be put up in ordinary straight, one cubic centimeter, amber glass vials with rubber stoppers sealed with paraffin, another vial of the same type to contain the glycerin necessary to dissolve the powder immediately before use. The vial is opened by removing the rubber stopper. The glycerin is poured into the vial containing the powder. The rubber stopper is tightly replaced and the contents are shaken for several minutes until the powder has mixed with the liquid. This simple and convenient way of putting up the dried vaccine may not be the best as far as preservation of the dried vaccine is concerned; sufficient moisture may penetrate into the vial to render the vaccine virus inert in less time than four months. It was therefore suggested that, in case the above-mentioned method will not give satisfactory results, the powder be kept in hermetically sealed ampules, or be kept on hand in open bottles placed in a small dessicator containing a hygroscopic chemical.

Besides the experiments already mentioned, we have arranged a field experiment by shipping dried vaccine virus to various places in the Archipelago and back, and then testing its activity on monkeys by vaccination. The places to which dried vaccine was shipped and tested when returned to Manila are: Currimao, Ilocos Norte; Pandan, Ilocos Sur; San Antonio, Zambales; Calapan, Romblon, Pasacao, Culion, Surigao, and Butuan; Cagayan and Iligan; Oroquieta and Dapitan; Zamboanga, Jolo, Cotabato, Quinimi, Glan, Davao, Agutay, and Cuyo. The length of time necessary for shipping and reshipping was twenty-five days. The animals vaccinated with these dried vaccines showed first-class "takes."

The process of drying the vaccine pulp seems to decrease its bacterial content. In the experiments above mentioned the bac-

terial content decreased three hundred sixty times during the process of desiccating.

It is hoped that this preparation will help a good deal in overcoming some of the difficulties with which health officers meet in eradicating smallpox in the Philippines.

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#### DR. GALLAGHER ON AVIAN TOXICOLOGY.\*

Dr. Gallagher, of the Pathological Division, Bureau of Animal Industry, has recently conducted some very interesting researches upon the susceptibility of fowls to various toxic substances. He finds that fowls which weigh between 3 and 4 pounds exhibit about the same susceptibility to poisons as do medium sized dogs. Fowls are, however, more resistant to calomel, strychnine, and tartar emetic and are less resistant to phenol, salicylic acid, and potassium cyanide.

The resistance of fowls to strychnine is very remarkable. Gallagher reports that 2 grains of the sulphate administered to a 5-pound bird were not toxic while this amount was lethal when given to a 3½-pound fowl, all doses given per os.

Tartar emetic was lethal in 15 grain doses and toxic in 10 grain doses; 3 grains of mercuric chloride were non-toxic, 4 grains killed in 3 days; calomel was non-toxic in 30 grain doses; fluid extract of ipecac was non-toxic in 45 minim doses, toxic in one dram and lethal in 2 dram doses; 1 to 2 grains of potassium cyanide were lethal while toxic effects were produced by ¼ to ½ grain. Potassium permanganate was lethal in 30 grain doses; salicylic acid was non-toxic in 15 grain, toxic in 30 grain, and lethal in 30 to 75 grain doses; 15 grains of santalin were non-toxic; 150 grains of sodium chloride was the toxic and lethal dose.

An interesting and important set of experiments revealed the facts that fowls are not visibly affected by drinking solutions of several remedies in the following concentrations: mercuric chloride, 1-6000, phenol 1-1000, potassium permanganate, 1-500 and crude catechu, 1-500, the solutions being furnished the birds for 18 to 21 days.

J. F. C.

\* *J. Am. Vet. Med. Assn.* v. 54: pp. 337-56, 1919.



## THE DIRECT IDENTIFICATION OF SOY-BEAN OIL.<sup>3</sup>

BY CHARLES A. NEWHALL,

SEATTLE, WASHINGTON.

Oil chemists seem to have overlooked a valuable test for the direct identification of soy-bean oil. Two color tests attributed to L. Settini<sup>1</sup> have been found of value in detecting admixtures of soy-bean oil with other commercial oils.

For some three years the writer has been using a modification of the second test, as follows: Five c. c. of chloroform are added to 5 c. c. of the oil, mixed in a small test tube with a few drops of gum arabic solution and 5 c. c. of a 2 per cent. solution of uranium nitrate or uranium acetate, and shaken to form a thorough emulsion. All samples of crude and refined soy-bean oil so far examined give a characteristic lemon-yellow emulsion; whereas, no other oil so far tested gives this color.

The most valuable use for the test has been in detecting admixtures of the cheap bean oil with high-priced wood oil or with linseed oil. With the former the test is sharp, it being possible to detect as low as 5 per cent. of bean oil.

With linseed oil the test is not so sharp, as linseed oil mixtures always give a slightly brownish color. It has never been absolutely certain that the linseed oil samples used for comparison were pure, and further work is in progress.

With such oils as peanut, cotton seed, sesame, rape, and coconut, the test is very sharp, and these oils give white or slightly colored emulsions with the uranium salt.

The yellow emulsion is not formed with bleached and deodorized bean oil, hydrogenated oil, or bean oil fatty acid.

This Settini test for bean oil is not as sharp as some of the direct color tests characteristic of sesame or cotton seed oils, but nevertheless it has been of great value in the commercial testing of oils, arriving from the Orient. This is no indication that it will work equally well with domestic soy-bean oil. Since the yellow emulsion seems to be due to the presence of coloring matter

\*From *Jour. Ind. & Engr. Chemistry*, Dec., 1920.

<sup>1</sup> *Chem. Abstr.* 7 (1913), 968.

in the crude oil rather than to some substance inherent to the oil, this coloring matter may be characteristic of only certain varieties of soy-bean. Until the exact nature of the yellow emulsion is cleared up, the Settini test should be used with caution, and its limitations taken into account.

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### FORMIC ACID IN THE BODY.\*

One of the scientific consequences of the menaces to human health which have arisen from the alarmingly frequent cases of consumption of methyl alcohol, or wood spirits, has been the more careful study of the behavior of this toxic substance in the organism. Methyl alcohol,  $\text{CH}_3\text{OH}$ , is not completely burned up to simple end-products in the organism; one of the products of its metabolism is formic acid  $\text{HCOOH}$ , as Pohl<sup>1</sup> demonstrated many years ago. The excretion of formic acid thus becomes an indicator of the fact that methyl alcohol has been taken into the body.<sup>2</sup>

It would be a comparatively simple plan to examine the urine for the presence of formic acid whenever information is sought as to possible instances of poisoning with wood alcohol. It happens, however, that formic acid has been known for many years to occur in the urine of persons living under supposedly normal conditions. Autenrieth<sup>3</sup> found that the daily output may approximate 0.25 gm., so that, without a quantitative measurement of the formic acid in the urine, definite conclusions as to its source and origin could not be drawn. The mere test for the presence of formic acid will not suffice to point to methyl alcohol as its predecessor.

Substantiation of this general conclusion has now been afforded by Stepp<sup>4</sup> at the Medical Clinic in Giessen. He has detected formic acid as a frequently recurring if not ever-present

\*From the *Jour. Amer. Med. Assoc.*, Dec. 4, 1920.

<sup>1</sup> Pohl, J.: *Arch. f. Exper. Path. u. Pharmacol.*, 31: 286, 1895.

<sup>2</sup> Methyl-Wood-Alcohol and Its End-products in the Body, editorial, *J. A. M. A.*, 74: 33 (Jan. 3, 1920).

<sup>3</sup> Autenrieth, W.: *Ueber den Ameisensäuregehalt des Harns, normalerweise und nach Eingabe verschiedener Substanzen*, München, *med. Wochenschrift*, Aug. 1, 1920, p. 862.

<sup>4</sup> Stepp, W.: *Ueber den Befund von Ameisensäure im menschlichen Blute*, *Ztschr. f. physiol. Chem.*, 109: 99 (Mar. 1, 1920).

constituent of human blood. Fifty years ago the Berlin physiologic chemist, Salkowski,<sup>5</sup> reported the presence, in this fluid, of a substance that was identical in behavior with formic acid, but the observation received little if any further experimental consideration. Among the persons whose blood was examined by Stepp were several diabetics. These afforded the surprise of yielding negative results. Little if any formic acid could be detected in their blood, which gave evidence of pronounced hyperglycemia. As the destruction of sugar is profoundly disturbed in such cases, Stepp has offered the tentative suggestion that formic acid may be a stage in the usual metabolism of carbohydrates—a stage that might not be represented when the normal transformations of the latter are interfered with. Thus, the problem of the physiologic significance of the traces of formic acid, commonly present in both blood and urine of man, has become a by-product, so to speak, of the investigation of the toxicity of methyl alcohol.

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## CURRENT LITERATURE

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### SCIENTIFIC AND TECHNICAL ABSTRACTS.

RESEARCH ON ANTISEPTICS.—Richet describes personal research on different antiseptics, estimating their potency by their action on the lactic ferment in milk. The vitality and activity of the ferment can be measured easily and with precision, by the amount of lactose transformed, that is, of lactic acid produced. The most striking feature of the results was the amazing potency of extremely minute quantities of the antiseptics. Even as little as ten thousandths of a milligram to the liter is not without action. He recalls that the phenomena of fecundation and immunization occur with quantities so minute as to be beyond our measuring instruments. Another fact brought out by his research is that whenever an antiseptic (and probably also a drug taken internally), has proved successful, then is the moment to change to another. As soon as the bacteria have had their proliferation checked by the antiseptic, change to another will continue the checking work, while if the same antiseptic is con-

<sup>5</sup> Salkowski; *Virchows Arch. f. path. Anat.*, 50: 174, 1870.

tinued, the bacteria rapidly adapt themselves to it. He announces as a guiding principle for all therapeutics, "Quand une médication a bien réussi, il faut l'abandonner et en adopter une autre."

We have seven excellent antiseptics at our disposal, he says, and nothing is easier than to use a different one for each day in the week, from phenol, sodium hypochlorite, tincture of iodine, silver nitrate, sodium fluoride and creosote to hydrogen dioxide. Another phenomenon brought out by his experiments is the strange irregularity in the action of certain antiseptics. When the same amount of milk is placed in a number of different tubes to ferment and conditions are made apparently identical in each, there will be a considerable variation in the amount of lactic acid produced in the different tubes. Sodium fluoride is the most regular in this respect, the yield in lactic acid being almost the same in the whole set of tubes, while mercuric chloride sometimes exaggerates the fermentation and sometimes checks it completely. (From *Médecine, Paris*; through *Jour. Amer. Med. Assoc.*, Nov. 6, 1920.)

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BIOLOGIC TEST OF VITAMINS.—Schaeffer advises testing the food in question by adding it to the J. C. Drummond test diet for white rats or white mice. On this diet the animals grow thin and finally succumb in forty or fifty days, but the addition of even 5 per cent. of a vitamin-containing food arrests the decline, and the animals begin to thrive with a suddenness actually amazing. He adds that the avitaminosis of young infants is the most common of all and is the hardest to differentiate. By this simple biologic test of the food the infant is getting, we can tell at once whether it is suitable for the infant or not. The Drummond diet comprises 18 per cent. purified casein; 56 per cent. purified dextrin; 3.7 per cent. of a synthetic saline mixture, and 20 per cent. chemically pure twice recrystallized lactose, with 2.3 per cent. agar. (From *Médecine, Paris*; through *Jour. Amer. Med. Assoc.*, Nov. 6, 1920.)

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VITAMINS IN COOKED CARROTS AND NAVY BEANS.—Miller states that cooking carrots at 100 C. for thirty minutes caused no reduction in the vitamin. Neither was there any destruction when carrots were packed tightly in a jar and heated at 115 C. for forty-five minutes. Cooking navy beans at 120 C. for thirty minutes de-

creased the vitamin content 40.6 per cent. In this case the beans were somewhat overcooked. Cooking navy beans in 0.5 per cent. sodium bicarbonate solution for 1 hour and 10 minutes caused a loss of 37.5 per cent. of the vitamin. A large proportion of the vitamin, from 36 to 70 per cent., was present in the cooking water. (From *Jour. Biological Chemistry, Baltimore*, through *Jour. Amer. Med. Assoc.*, Nov. 13, 1920.)

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NEW METHOD OF ESTIMATING QUININE.—(C. Bamberger—*Pharm. Zentralb.*, 1920, 61, 257-259; through *Chem. Zeit.*, 1920, 44, Rep. 223.)—Two and a half grms. of cinchona bark are heated for ten minutes over the water-bath with two c. c. of hydrochloric acid and 20 c. c. of water, and the mixture then cooled, shaken with 25 grms. of chloroform and 50 grms. of ether, and treated with 5 grms. of sodium hydroxide solution. The contents of the flask are vigorously shaken (about 300 times) within two to three minutes, and treated with sufficient plaster of Paris (about 40 to 50 grms.) to clarify the liquid, and 60 grms. of the clear chloroform-ether layer transferred to a separating funnel. It is shaken twice (for two minutes each time) with 5 c. c. of  $\frac{N}{10}$  hydrochloric acid and twice with 10 c. c. of water, and the extracts united and titrated with  $\frac{N}{10}$  potassium hydroxide solution, methyl red being used as indicator. The results agree closely with those obtained with the Swiss Pharmacopœia method, and the methods of Frerichs and Mannheim. (From *The Analyst*, November, 1920.)

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DETERMINATION OF THE JELLYING POWER OF GELATINS AND GLUES BY THE POLARIMETER.—C. R. Smith (*J. Ind. and Eng. Chem.*, 1920, 12, 879).—The optical rotation of solutions of all gelatins and glues at 35° C. is practically constant, ranging from—6.70 to 7.20° Ventzke per gm. of solid material, but on cooling to 15° C. the rotation increases proportionately to the viscosity of the solution. Increase in concentration gives higher values, but by keeping the solutions for several hours at 15° C. a gradual decrease is observed, so that solutions of all strengths under the above working conditions yield a constant rotational value for any

particular sample. Determinations of the polarimetric values are made by soaking 3 grms. of the powdered air-dried gelatin in cold water for 30 minutes, immersing in a boiling water bath until solution is complete, cooling to 35° C. and diluting to 100 c. c. If clarification is necessary, 5 grms. of light magnesium carbonate are added to the solution, which is kept at 30-40° C. for an hour, and filtered bright. The first rotation is measured in a 200 mm. tube at 35° C., the solution then being kept at 15° C. over night, and the rotation again observed next day. The results are expressed by the formula  $\frac{\text{Rotation at } 15^{\circ}}{\text{Rotation at } 35^{\circ}}$ , and are inversely proportional to the percentage of gelatin required to produce a standard jelly at 15° C. This standard is defined as a solution of such strength that a bubble of air 4 to 5 mm. diameter admitted to the polarimeter tube moves vertically with a motion of 4 cm. per second. Two tables are provided, giving a large number of results obtained, and a third one showing the comparison between the polarimetric values and jelly strengths obtained in the following manner: A 60° funnel is partly filled with mercury, 50 c. c. of the gelatin solution are poured upon the surface, and allowed to set at 10° C. The mercury is then run out, and a partial vacuum of 600 mm. of water produced below the jelly, when the depression of the upper surface is measured by a micrometer gauge. The results obtained by this method bear a moderately definite ratio to those given by the polarimetric method. (From *The Analyst*, November, 1920.)

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POISONOUS PROPERTIES OF YEW.—There can be no doubt about the poisonous properties of the yew; all parts of the plant but the arillus have been shown to be poisonous. Yew has caused the death of many horses and cattle, while asses, mules, deer, pigs, rabbits, and pheasants have also been poisoned. In "Plants Poisonous to Live Stock," by H. C. Long, the question is dealt with at considerable length, and while the author produces much evidence against the plant, he reminds us that many cases have been recorded in which fatal results have not followed the ingestion of the leaves, for it appears that the lower branches of yew trees in parks are constantly cropped by cattle without ill-effects. The old leaves or shoots are mentioned as being the most poisonous parts. Eaten by an

animal on a full stomach a small quantity of yew may cause little or no dangerous results. The poisonous principle is generally considered to be taxine, an alkaloid having the composition  $C_7H_5NO_{10}$ . It is a question, however, whether it is the *only* poisonous constituent. The yew is irritant and narcotic, and the poison is not cumulative, but, on the other hand, rapidly effective, so that animals may die apparently suddenly, no previous symptoms having been observed. In an interesting illustrated article entitled "Poisonous Berries," by E. M. Holmes, F. L. S.; which appeared in the P. J. of November 20, 1915, page 638, it is shown under what conditions the leaves or fruit may be poisonous or not. (From *The Pharm. Jour. and Pharmacist*, Sept. 4, 1920.)

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POISONING BY FLUORIN COMPOUNDS.—Kockel and Zimmerman report two cases of poisoning from hydrofluoric acid. The clinical picture was characterized by marked physical weakness and frequent vomiting. The course of the intoxication was very rapid, covering not much more than two hours before the fatal issue. One case was traced to rat poison and is regarded as a suicide; the other was a criminal poisoning case. (From *Munchener medizinische Wochenschrift*, Munich, through *Jour. Amer. Med. Assoc.*, Nov. 6, 1920.)

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## MEDICAL AND PHARMACEUTICAL NOTES

URSONE IN ERICACEOUS PLANTS.—The author has examined a number of plants belonging to the natural order Ericaceæ for ursone and found it in all of them; hence he concludes that it is of general occurrence in Ericaceæ. The best method of isolating it is that of Dodge (*Jour. Amer. Chem. Soc.*, 40, p. 12). It was identified by ultimate analysis and also by the following color reactions: (1) With sulphuric acid it gives an orange-yellow liquid with a green fluorescence; (2) a little dissolved in 2 c. c. of acetic anhydride gives with 8 or 10 drops of sulphuric acid a red coloration passing to violet, green, and blue; (3) a little dissolved in chloroform, and shaken with an equal volume of sulphuric acid, colors the latter yellow. Ursone was also found in holly, maté, and the leaves of two other species of *Ilex*. It crystallizes in white needles, melting at  $273^{\circ}$ . One gm. is soluble in 178 gms. of ethyl

alcohol, 88 of methyl alcohol, 388 chloroform, 1675 of carbon disulphide, 192 of ethylene bromide, 140 of ether, and 35 of boiling alcohol. Optical rotation  $[\alpha]_D^{13} = 58^\circ$ . It can be titrated with alkalies as well as with acids. The formula is  $C_{29}H_{47}O \cdot COOH, 2H_2O$ . It yields a readily crystalliable methyl ester. (From *Pharm. Weekblad*, vol. 57, p. 1128, through *The Pharm. Jour. and Pharmacist*, Oct. 30, 1920.)

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STAINING RETICULATED CELLS.—Permanent preparations are made by Cunningham by combining a vital with a Wright's stain. The reticulation is as clear, if not clearer, than by the older methods, and the Wright's stain retains all its differential qualities, except the polychromatophilia, which is not present. The ease and simplicity of this method brings the study of reticulated erythrocytes within the scope of routine blood examination. A small drop of a 0.3 or 0.5 per cent. aqueous or alcoholic solution of brilliant cresyl blue is placed on the end of a clean slide or the center of a cover glass and smeared around over an area 1.5 cm. in diameter. Next, a drop of fresh blood is placed on a clean coverslip and dropping it face down on one of the areas of dried stain. The stain goes into solution almost instantly. The cover glasses, or slide and cover glass, are now pulled apart as in making an ordinary blood smear and are permitted to dry. On drying, the blood turns a dirty greenish blue color. The slide or cover glass is then stained with Wright's blood stain. The preparation is dried in the usual manner and mounted with Canada balsam. The reticulum is stained a deep or light blue, depending on its density, and gives a striking picture in its contrast with the pink protoplasm of the cell. (From *Archives of Internal Medicine, Chicago*, through *Jour. Amer. Med. Assoc.*, Nov. 13, 1920.)



# THE AMERICAN JOURNAL OF PHARMACY

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## EDITORIAL

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### AN INSPIRATION.

Not the least important of the attributes of the human intellect implanted by the Creator is inspiration. This is a dual faculty possessing the power alike of receiving and of imparting elevating influences. Some particular occurrence in the career of an individual may make a deep and lasting impression and in some manner, often unexplainable, prove to be the inspiration to a higher ambition and to accomplishments that were considered as beyond his ability. The success that he achieves is not limited to himself, but becomes an inspiration to others, an example that may stimulate many to a nobler and progressive life-work.

What is true of the individual applies with still greater force to events that influence the developments in any of the lines of human endeavor, whether these be in the political, professional, industrial or social arenas. A single event may have an influence upon the future development of an entire calling, or even of the nations of the world, that cannot be foreseen.

The celebration of the Founders' Day by the Philadelphia College of Pharmacy and Science is an occurrence of more than passing interest. The lessons and the inspiration radiating from the ceremonies associated with this centennial, like unto the event that it commemorated, must have a permanent influence toward the advancement of the profession of pharmacy.

Upon such an occasion it is natural for the participants to reflect and bring in mental review the occurrences of one hundred years ago and to conceive some idea of the motives and thoughts that actuated the prime movers in the events that led to the creation of the Philadelphia College of Apothecaries, the first pharmaceutical

society organized in the new world. The gradual evolution of the practice of pharmacy in America, its condition at that time and at least some of the errors and frauds that had crept into the drug business at that period along with the particular action of the trustees of the University of Pennsylvania that inspired the worthy druggists and apothecaries of the City and Liberties of Philadelphia to organize themselves into a college, are matters that have been fully recorded. From a perusal of these records it does not appear that the men who were active in the movement had given very much thought to the possibilities and influences that might flow from their action or had a vision of what the result of their efforts would mean to the future of pharmacy. The existing conditions inspired them to take action in accordance with their deliberate judgment and to establish an institution whose example and labors have been of incalculable value in the development of the profession in which they were engaged and, likewise, in the benefits accruing to the public. Their efforts have been a continuous inspiration extending throughout the century that has past and their achievements remain with us and the coming generations not alone as historical records of accomplishments but, likewise, as potent influences. The inspirations of the century that is closing are an enduring foundation for renewed energies and still higher aspirations.

The inspiration growing out of this centennial celebration of the founding of pharmaceutical education in America should be of sufficient magnitude and of such potent influence that the pessimistic views that have found expression as a passing fad among *quasi* pharmacists should be forever drowned out. The first century of pharmaceutic education has left a firm and well built foundation, and the achievements of the past and the plans for the future are inspirations for an unprecedented progress and our imagination pictures a magnificent addition to the temple of pharmacy erected long before the close of the second century.

G. M. B.

## ORIGINAL PAPERS

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### FOUNDERS' DAY CELEBRATION.

The One Hundredth Anniversary of the founding of the Philadelphia College of Pharmacy and Science was celebrated on February 23d, by appropriate exercises. The lecture rooms, the various laboratories, the museum and the library were open to public inspection and numerous visitors viewed the extensive exhibits, and were surprised to note the extent of the collections and equipment.

In the afternoon a number of the descendants of the founders of the College, the present officers, faculty members and many of its friends gathered in the library. Shortly after two o'clock they proceeded by automobile to Carpenters' Hall, where a special meeting of the College was held. The commemorating services here were opened by President Howard B. French calling the meeting to order, and reading from a copy printed in 1821, the preamble and constitution adopted by the Philadelphia College of Apothecaries.

Then the Secretary of the College, Dr. Charles A. Weideman, read from the original minutes the transactions of the meeting held in this historic building by the druggists and apothecaries of the City and Liberties of Philadelphia on February 23, 1821, and the subsequent meetings held on March 13, 1821, and two weeks later, at which the first officers and trustees of the College were elected.

This was followed by a brief address by George M. Beringer, Chairman of the Board of Trustees, in which the work of the founders of the College was referred to; the history of the organization; its endeavors and progress for the past century; and its aims and hopes for future developments were outlined.

Charles Marshall, a direct descendant of Charles Marshall, the first president of the College, was present at these exercises. Likewise Henry Troth, a grandson of Henry Troth, one of the founders, and Wm. S. Ellis, a grandson of Charles Ellis, one of the original members.

Those in attendance at Carpenters' Hall signed a roll book as a permanent record of the attendance. At the close of the meeting,

a moving screen picture was taken of Carpenters' Hall and the audience leaving, and this will likewise be preserved as a historical record of the event.

In the evening, the main commemorative services were held in the College auditorium. This room and the gallery were filled with members, friends, students and alumni, gathered to pay tribute to the founders and the achievements of the past century.

President French welcomed the guests, many of whom had come from New York, Washington, Baltimore and other distant places, and stated the purpose of the gathering.

Dean Charles H. LaWall then read a paper on the founding of the Philadelphia College of Pharmacy and Science, in which the events which led up to the initial meeting and the formation of the College were related.

The next speaker of the evening was Prof. Henry Vin Arny of the College of Pharmacy of Columbia University, New York City. The title of his address was "Pharmacy 100 Years Ago."

As Prof. Arny ceased speaking, Mayor Moore arrived, and when he was introduced by the chairman, received a hearty ovation. In the course of his remarks the Mayor referred to the efficient work in behalf of humanity that this College has performed. He said "That this school has lived for 100 years proves its endurance and its quality." He promised his personal assistance and influence in seeing that the Philadelphia College of Pharmacy and Science is moved from its present location to a more desirable one. He declared that "It is wonderful to think of the world-wide influence of this institution from whose walls have gone forth not only men, but thoughts, the contributions of genius. The College should not have remained in its present environment so long. It should have been moved years ago. I can only hope that in some way the Mayor, long before his retirement from office, may be able to assist in having this institution housed in a building more suitable for a school of its dignity and service. This is due the College for the work it has performed and for the sake of its splendid student body."

The remarks of the Mayor were construed as showing his purpose to co-operate with the officers of the College in endeavoring to secure a site for the new buildings on or near the Parkway.

The closing address of the evening was made by Prof. Samuel P. Sadtler, Emeritus Professor of Chemistry of the Philadelphia

College of Pharmacy and Science. His topic was "The Influence of Pharmacists on the Development and Advance of Modern Chemistry." These addresses are published in full in this number of the JOURNAL.

A pleasant feature of this celebration was the numerous congratulatory letters and telegrams that were received from all parts of the country. President French read some of these to the audience. Space permits the reproduction of but a few:

"University of Pennsylvania,  
February 23, 1921.

Howard B. French, Esq.,  
The Philadelphia College of Pharmacy and Science,  
Philadelphia, Pa.

My dear Mr. French:

I find on my desk a little pamphlet, containing the programme of the exercises commemorative of the Centennial of the Philadelphia College of Pharmacy and Science. I regret exceedingly that it will not be possible for me to attend any of the various exercises. Will you please accept from me, both officially and personally, my hearty felicitations on the rounding out of a hundred years of the splendid work that has been done by the institution over which you preside?

Sincerely yours,

(Signed) JOSIAH H. PENNIMAN."

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"St. Louis College of Pharmacy,  
St. Louis, Mo., February 14, 1921.

Mr. Howard B. French, President,  
The Philadelphia College of Pharmacy and Science,  
Philadelphia, Pa.

Dear President French:

First of all, permit me to sincerely thank you for remembering me with an invitation to the Centennial Celebration of Founders' Day of the Philadelphia College of Pharmacy and Science.

I regret that I do not see my way clear to be present in person, but you may rest assured that I shall be there in spirit.

I have the honor of holding the degree of Ph. M. from the

College and have, for many years, been acquainted with the institution and appreciated the good work your school is doing.

I trust that your observation of the Centennial, February 23, 1921, will be pleasant and successful in every particular.

Yours very truly,

(Signed) H. M. WHELPLEY, *Dean.*"

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"St. Louis, Mo., Feb. 23, 1921.

Howard B. French, President,

Philadelphia College of Pharmacy and Science,

Philadelphia, Pa.

Congratulations and best wishes from the St. Louis College of Pharmacy on your Centennial Celebration.

GEORGE R. MERRELL, *President.*"

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"Atlanta, Ga., Feb. 23, 1921.

Philadelphia College of Pharmacy and Science,

Philadelphia, Pa.

We who have retained our love and friendship for the Philadelphia College of Pharmacy and Science, and will always hold a pride for her traditions and feel ever rejoiced at her progress and welfare, beg to join our names to those who are celebrating the Hundredth Anniversary of our Alma Mater.

JOSEPH JACOBS (1879).

SINCLAIR SARTORIOUS JACOBS (1909)." 

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"New Orleans, La., Feb. 23, 1921.

Prof. S. P. Sadtler,

145 North 10th Street,

Philadelphia, Pa.

Congratulations to my Alma Mater on its Hundredth Anniversary. May P. C. P. & S. live forever is the wish from sunny south.

ADAM WIRTH."

Ann Arbor, Mich., Feb. 21, 1921.

Dean Charles H. LaWall,  
Philadelphia College of Pharmacy and Science,  
Philadelphia, Pa.

The College of Pharmacy of the University of Michigan congratulates the Philadelphia College of Pharmacy and Science most cordially upon the One Hundredth Anniversary of Founders' Day to be celebrated on Wednesday of this week. The contributions of your College to American Pharmacy during the past century have indeed been remarkable. May your future be as brilliant as your past has been illustrious. We regret exceedingly that we cannot be represented by some member of our faculty.

EDWARD H. KRAUS, *Acting Dean.*"

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Havana, Cuba,  
February 22, 1921.

Mr. Howard B. French,  
Philadelphia College of Pharmacy and Science,  
Philadelphia, Pa.

Our heartiest congratulations to the mother of American Pharmacy on her Centennial Celebration. May the good work of its founders and those who followed them for the past hundred years be the guiding light to the younger generations and help them maintain her standard *The First College of Pharmacy in the World.*

PROF. JOSE P. ALACAN.

MISS SILVIA C. ALACAN (1915)."

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Madison Wis., February 21, 1921.

Philadelphia College of Pharmacy and Science,  
Philadelphia, Pa.

Please accept hearty congratulations of University of Wisconsin and its Department of Pharmacy upon being the first institution to have completed a century of activities of usefulness and advance in pharmaceutical education along the various lines of the profession. May the knowledge of the past achievements stimulate your present and future associates to continued effort during the century just starting.

E. A. BIRGE."

"The Pennsylvania State College,  
State College, Pa., February 18, 1921.

Mr. Howard B. French, Pres.,  
Philadelphia College of Pharmacy and Science,  
Philadelphia, Pa.

My dear Mr. French:

Permit me to thank you for your kind invitation to be present at the Centennial Celebration of Founders' Day of the Philadelphia College of Pharmacy and Science on the 23rd instant. My conditions prevent my personal acceptance of the invitation, but I trust that you may have a very enjoyable occasion and that it may serve to bring to the mind of the public the very important contributions which the College has made to American pharmacy.

Very cordially,

(Signed) WILL FREAR."

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"Massachusetts College of Pharmacy,  
Boston, Mass., February 21, 1921.

Philadelphia College of Pharmacy and Science,  
Philadelphia, Pa.

Gentlemen:

Your kind invitation for me to attend the Centennial Celebration of Founders' Day on Wednesday, February 23, is received, and it is only because of an important prior engagement on the same date that I am compelled to send my regrets. I hope to be able to attend the main centennial celebration in June, if honored with an invitation to them.

We all rejoice at the long and honorable record of achievement made by your institution and hope for even greater things from you in the future.

With my best wishes for the success of the Celebration, I am,

Yours very truly,

(Signed) THEODORE J. BRADLEY, *Dean.*"



"Western Reserve University,  
Cleveland, Ohio, February 15, 1921.

Dr. Charles H. LaWall,  
145 North 10th Street,  
Philadelphia, Pa.

Dear Dr. LaWall:

I am in receipt of the invitation of the Philadelphia College of Pharmacy and Science to attend the Centennial Celebration of Founders' Day.

I only wish that I could attend and meet many of the men and women who will bring back memories of early pharmacy to Philadelphia. I know that I could learn much and derive a great deal of enthusiasm from my work by being present at such a gathering. I know that it will have the same effect of giving enthusiasm to the members of your faculty and go far towards bringing future success to your College. I am ever,

Sincerely yours,  
(Signed) EDWARD SPEASE."

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"1525 Walnut Street,  
Philadelphia, Pa.,  
February 14, 1921.

Mr. Howard B. French, President,  
Philadelphia College of Pharmacy and Science,  
Philadelphia, Pa.

My dear Mr. French:

Thank you very much for your kind invitation to attend the Centennial Celebration of Founders' Day.

The Philadelphia College of Pharmacy and Science has an honorable and enviable record. Its great teachers and its wise and progressive board of trustees have, I verily believe, done more for the advancement of pharmacy as a profession than any other single agency of which I have knowledge.

The United States Pharmacopœia and all that it stands for in the way of scientific progress is in large measure the product of the scientific zeal, the indefatigable industry and the broad outlook of men identified with the Philadelphia College of Pharmacy and Science and their influence upon pupils and confreres associated in the work.

Permit me to congratulate you and your colleagues of the trustees, as well as the faculty and alumni association, and to wish for the future a glory that shall surpass that of former days.

I trust to be present at the Celebration, but send this letter, so that should I be unavoidably prevented, you will know that it is not from want of appreciation either of the College, or of your courtesy.

Sincerely yours,

(Signed) S. SOLIS COHEN."

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"St. Louis, Mo.,

February 23, 1921.

Prof. Charles H. LaWall,

Philadelphia College of Pharmacy and Science,

Philadelphia, Pa.

*The Meyer Druggist* and many other friends of your school here join in felicitations on the Centennial of Founders' Day of your historic institution.

HENRY M. WHELPLEY, *Editor.*"

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"Medical College of Virginia,

Richmond, Va., February 15, 1921.

Dr. Charles H. LaWall,

Philadelphia College of Pharmacy and Science,

Philadelphia, Pa.

Dear Dr. LaWall:

I thank you for the invitation to attend the Centennial Celebration of the Philadelphia College of Pharmacy. I sincerely trust that the occasion will be profitable and pleasant, as I know it will be. It would certainly give me much pleasure to have a share in so important an event in the history of an institution which has had so great a part in pharmaceutical education in America.

With best wishes and kind personal regards for yourself and your co-workers, I am,

Sincerely yours,

(Signed) WORTLEY F. RUDD,

*Dean, School of Pharmacy."*

"Parke, Davis & Company,

Detroit, Mich., Feb. 16, 1921.

Mr. Howard B. French, President,

Philadelphia College of Pharmacy and Science,  
Philadelphia, Pa.

Dear Mr. French:

In this afternoon's mail I have received an invitation to the Centennial Celebration to be held at the Philadelphia College on February 23. I am honored to be among the invited, and I sincerely regret that circumstances will prevent me from being present. Mr. Bartlett is out of town and I cannot very well get away until his return.

You will receive hundreds of compliments on the arrival and conduct of such a celebration. One more or less doesn't particularly matter, and yet I want to add my meed of praise to the Philadelphia College. No other institution can boast of such a long history, and none has such a bright galaxy of stars in the firmament represented by its alumni. Our late president, Mr. Ryan, would be intensely interested in the event if he were still with us, and once more we are reminded of the great loss which we have all suffered in his death.

I wish it were possible to be present on the 23rd. I shall be with you in spirit, and I sincerely trust that the affair will go off with all the sentiment and brilliance which are characteristic of the Philadelphia College of Pharmacy and Science.

Very sincerely yours,

(Signed) HARRY B. MASON,

*Secretary.*"

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"Purdue University,

Lafayette, Indiana, February 15, 1921.

Mr. Howard B. French, President,

Philadelphia College of Pharmacy and Science,  
Philadelphia, Pa.

Dear Mr. French:

Permit me to sincerely thank you for the kind invitation to be present at the Centennial Celebration of Founders' Day. I am sorry to say that it will not be possible for me to attend

this celebration. Permit me, however, to extend to you and the College my sincerest wish for another hundred years of such excellent service as your College has rendered to our profession.

Very truly yours,

(Signed) C. B. JORDAN,  
*Director, School of Pharmacy."*

"Johns Hopkins University,

Baltimore, Md., February 14, 1921.

Mr. Howard B. French,

Philadelphia College of Pharmacy and Science,

Philadelphia, Pa.

Dear Mr. French:

I regret very much that circumstances prevent my attendance at the Centennial Celebration of Founders' Day of the Philadelphia College of Pharmacy and Science. I have always prized very highly my honorary membership in the College. Certainly, no other institution of our country has had so great an influence on the development of pharmacy, as well as the allied sciences, as has the Philadelphia College of Pharmacy and Science. Please accept my best thanks for remembering me with an invitation on this great occasion.

Very sincerely yours,

(Signed) JOHN J. ABEL."

"Cincinnati, Ohio,

February 23, 1921.

Philadelphia College of Pharmacy and Science,

Philadelphia, Pa.

The Cincinnati College of Pharmacy through its officers and faculty extends hearty greetings on its one hundredth anniversary of service and as the founder of true American pharmacy and we trust that truth, honor and science in pharmacy of the past may find equal prominence at the next centenary of Philadelphia College of Pharmacy and Science.

F. S. KOTTE, *President.*

WALTER R. GRIESS, *Dean.*

JOHN URI LLOYD.

CHARLES T. P. FENNEL."

## THE FOUNDING OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.\*

By CHARLES H. LAWALL, Ph.G. (1893), Ph.M. (1906),  
*Dean and Professor of Pharmacy,*  
*Philadelphia College of Pharmacy and Science.*

We of the present are met together upon this Centennial occasion to do homage to those of the past. The debt to the Founders of the Philadelphia College of Pharmacy and Science is not ours alone. It is society's debt which we, as co-sharers in the benefits which have resulted from that act, are privileged to repay in part by ceasing from our present labors for a time in order that we may bring proper tribute to the memory of those men and do justice to their accomplishments.

America one hundred years ago was a sparsely settled country, with few and difficult means of intercommunication between distant points, neither railways nor canals having yet appeared.

Philadelphia one hundred years ago was the largest and most important city in these United States, which had yet to celebrate their semi-centennial as a nation.

To properly appreciate the atmosphere in which these men lived and the difficulties under which they labored we must refresh our minds regarding some of the material changes that have taken place since that time.

A glimpse at a Philadelphia city directory for 1821 will give us an impression of the period through certain occupations which are listed with frequency, and which are missing in a directory of today. *Bleeder and Barber* is one of the noteworthy instances of a peculiar occupation which continued even beyond that period, reminding us that the surgeon was not necessarily a medical doctor, nor even a person of education. This is perpetuated in the red and white striped barber pole of today, then the advertising sign of the bloodletter.

*Sea Captain, Mariner, Shipwright, Sailmaker* are redolent of the days of wooden sailing ships, then supreme upon Poseidon's realm and just beginning to be displaced by steamboats upon the inland waters of our eastern coast.

\*An address delivered at the Centennial Celebration of Founders' Day, February 23, 1921.

*Chimney Sweep, Sweep Master, Tallow Chandler* are reminiscent of the open hearth wooden fires and the meagre illuminating facilities of a period antedating the use of coal or kerosene for heating or lighting.

*Carter, Cordwainer, Fishmonger, Ostler, Scrivener, Soap-boiler, Tavern Keeper, Victualler, White Smith and Woodsawyer* each carry evidence of the close association of the language of that time with the mother tongue of England.

*Pepperpotmaker* is an occupation confirming the early origin of Philadelphia's gastronomic distinctiveness which is still acknowledged in some directions.

Friction matches had yet to be invented. Daguerre had not yet practiced his art of reproducing likenesses, hence the only pictures we have of the founders who died before 1840 are from oil paintings or miniatures. Gold had yet to be discovered in California, and oil in Pennsylvania. Elias Howe had not yet invented the sewing machine.

Letter postage ranged from six cents to twenty-five cents for a letter of a single sheet of paper, depending upon the distance it was carried.

The first train of railway cars had yet to run, while the telegraph, telephone and typewriter were in the dim and misty future. Percolation had not been suggested for drug extraction. Alkaloids were of such recent discovery that they were still called vegetable alkalies.

The work of Liebig, Berzelius, Wöhler and Pasteur was still to be done.

Heat was discussed as a material substance in the works in physics and was usually called caloric.

Professional and scientific interest and education was just awakening along certain lines.

The University of Pennsylvania had established its Medical School a bare half-century before and was then conducting a three-year course, attended by several hundred students, and numbered among its professors such distinguished men as Dr. John Redman Coxe, Dr. Robert Hare, Dr. Philip S. Physick, and Dr. W. C. P. Barton. The course in Natural Sciences at this same Institution had not yet emerged from the difficulties which attended the teaching of science at a time when science and irreligion were looked upon as synonymous by many. In that department the professors

received no salaries and were required to furnish their own apparatus and specimens and were not considered members of the faculty.

There was no distinct department of Chemistry at the University, the instruction in that branch being given in connection with medicine. A memorial which had shortly before been presented to the Trustees of the University of Pennsylvania, signed by Drs. Rush, Wistar, Barton and Physick, is worth quoting in full to illustrate the field which chemistry was then supposed to cover :

"It is peculiarly expedient that the Professor of Chemistry should have a full and extensive knowledge of medicine, because very many valuable articles of the *materia medica* are derived from chemistry and the nature of these articles can only be understood by a person who has a competent knowledge of both chemistry and medicine. The students of medicine who almost exclusively support the Professorship of Chemistry are induced to do so in consequence of its application to Pharmacy and the different branches of medicine. No man can teach Pharmacy unless he has some knowledge of the practice of medicine and the application of chemistry to physiology and the other branches of medical science can only be taught by a chemist who understands them."

The chair of *Materia Medica* in the University was changed in 1818 to the chair of *Materia Medica* and Pharmacy, which was continued unchanged in title for many years. A similar change had occurred some years before, but had been abandoned. All final examinations for a doctorate degree were conducted orally and often before the Trustees of the Institution. Each applicant was required also to publicly defend his thesis, which was an original dissertation required as part of his collegiate work.

Text books and reference books on Chemistry were fairly numerous even then, but none had appeared in which the use of chemical symbols simplified the teaching of reactions. Some of the most popular treatises of the day on Chemistry were in the style of "conversations," a stilted and prolix form which has no counterpart today. "Chemical Amusement" was the title of another book of the period. This was written by Frederick Accum, who is noted as the author of "A Treatise on Adulterations of Food, and Culinary Poisons" published in Philadelphia in 1820, one of the earliest treatises of its kind.

James Cutbush, concerning whose work and character Dr. Edgar Fahs Smith has contributed a most interesting monograph, was an early Philadelphia Chemist and Apothecary who published

many articles of interest and value upon chemical subjects, beginning with 1808.

He was in business at 25 South Fourth Street in 1819, and as early as 1812 had advertised a course of "Evening lectures on Chemistry" and also "Lectures on Theoretical and Practical Pharmacy." For this latter course a fee of twenty (20) dollars was charged. This course was evidently neither popular nor successful, for no further reference is found relating to it, although Mr. Cutbush attained the distinction of being appointed Assistant Apothecary General in the U. S. Army on August 12, 1814. The duties of this office must have kept him busy in this vicinity for in the Philadelphia Directory of 1821 he is listed as "Assistant Apothecary General of the U. S. Army, residing at 207 South Fourth Street."

Conditions in Pharmacy at that period had not been satisfactory to many of the medical practitioners of the period, nor to the leading apothecaries, as they were then officially termed. The practice of writing prescriptions had been established in Philadelphia about 1765 by Dr. John Morgan, who, upon returning from the completion of his medical studies in Europe, had been accompanied by an accomplished apothecary from Great Britain, named Leighton, who brought with him a large assortment of medicines. This first prescription store in Philadelphia did not long survive the antagonism of local physicians and pharmacists, and it is stated that even at the close of the American Revolution there were only three medical practitioners in Philadelphia who confined their practice to prescription writing.

An unsuccessful attempt was made in 1789 to interest American medical men in the establishment of a national Pharmacopœia in which Dr. Samuel Powell Griffiths, of the University of Pennsylvania, took a prominent part.

Through ignorance and carelessness certain abuses crept into the early drug business primarily because there was neither control from without nor inspiration from within. Patent medicines became numerous, most of them being founded upon the prescriptions of successful physicians, for it must be remembered that a prescription was at that time believed to be a combination of medicaments satisfactory for the relief of disease without the necessity of modification or alteration to suit the particular individual as is the scientific and approved practice today.



Indeed, at that time, the most eminent of medical practitioners allowed their names to be attached to "Formularies" which purported to contain the successful recipes and prescriptions from the most celebrated physicians of this country and Europe. Many of our official compound preparations of today, still widely used, are prescriptions of illustrious practitioners of the past. Among these are Dover's Powder, originated by Dr. Thomas Dover of England, about 1725; Huxham's Tincture, by Dr. John Huxham of England, in 1755; Fowler's Solution, by Dr. Thomas Fowler of England, in 1786; Blaud's Pills, by Dr. J. Blaud of France, in 1831; Coxe's Hive Syrup, by Dr. John Redman Coxe, about 1810; and Jackson's Pectoral Syrup, by Dr. Samuel Jackson, about 1835; and many others might be given. One of the serious conditions which occurred at that time was the prevalence of adulteration of drugs and medicines, and of substitutions. Indeed, one earlier authority published an entire work upon the latter subject called "*Quid Pro Quo*." Another in an American work published in 1818, justified substitution in certain cases as follows:

"First, for persons who haggle over price and care not for quality, and

Second, for those who are bad pay, to compensate for the risk of loss," and accompanied this advice with an approved list of substitutes for certain drugs.

The culmination of the feeling regarding this condition was reached early in 1821, when the University of Pennsylvania took steps leading toward the establishment of a course in Pharmacy, at the request of the medical faculty.

Resolutions were passed by the Board of Trustees of the U. of P. on February 21, 1821, in which announcement was made of the intention to establish a course of instruction in pharmacy and to confer the honorary degree of Ph. M. upon certain prominent apothecaries of the city at that time.

Prior to this, however, the Trustees of the University had received an application in 1816 from Dr. James Mease, a Philadelphia physician, to conduct a course of lectures in Pharmacy. This permission had been granted, but it is probable that no applicants appeared to take the course, for no further mention was ever made of it.

The Philadelphia Apothecaries learning of the action of the University Trustees, on February 21st had their self-respect challenged by the move to conduct a course in Pharmacy without first

consulting the apothecaries themselves, and as tradition has it, the two individuals directly responsible for the protest which was voiced at the meeting held in Carpenters' Hall, on the day whose centennial we are celebrating, were Peter Lehman and Henry Troth, the former a retailer, the latter a wholesale druggist of prominence at that time.

On February 23, only two days after the publication of the resolutions adopted by the University of Pennsylvania Board of Trustees, the initial meeting of the Founders of this College was held. We do not know the complete list of those in attendance, but we know that Stephen North was made Chairman, and Peter Williamson, Secretary, and resolutions were prepared and offered, and after some debate were adopted and referred to a committee, who were given power to call a subsequent meeting "at such time and place as they deem proper."

This special committee was noteworthy for the character and standing of its members. The names are as follows:

Samuel Jackson, M.D.	40 N. Fourth Street
Daniel B. Smith	33 High (Market) Street
Robert Milnor	161 S. Second Street
Peter Williamson	Second and Almond Street (below Bainbridge Street)
Stephen North	14 N. Second Street
Henry Troth	222 High (Market) Street
Samuel Biddle	142 High (Market) Street
Charles Allen	160 S. Second Street
Frederick Brown	with Chas. Marshall, 56 Chestnut Street

These street numbers are under the former system and bear no direct relation to present locations.

SAMUEL JACKSON was then 34 years of age, and had been associated with his father and brother in the drug business. He became the first Professor of Materia Medica and Pharmacy, resigning in 1827 to take a similar chair later at the University of Pennsylvania, where he continued until his death in 1872. He was one of the most illustrious of practitioners and teachers of medicine of his time. He was President of the first Philadelphia Board of Health, which had as its secretary the renowned

Franklin Bache, later Professor of Chemistry in our College. It was Dr. Jackson who first suggested the present name of the Philadelphia Academy of Natural Sciences, and that organization celebrates its Founders' Day on the anniversary of the date upon which this name was adopted, the previous meetings having been informal gatherings. It is a curious commentary on the period that Dr. Jackson was not at the time a member of the group of men who formed the Academy, because being a rising young medical practitioner he could not afford the inference of irreligion which attached to those who were too deeply interested in natural science.

DANIEL B. SMITH was a young man of 29 at the time of this meeting. He had learned the drug business with John Biddle of Philadelphia, and had entered business for himself at Sixth and Arch. Later the firm name was Smith & Hodgson, who were subsequently succeeded by Bullock and Crenshaw. In 1820, he aided in the establishment of the Apprentices' Library. He was the Chairman of the first publication committee of the *American Journal of Pharmacy* and a frequent contributor of valuable papers. He was one of the original members of the Franklin Institute, and one of the incorporators and the first corresponding secretary of the Pennsylvania Historical Society. He was one of the incorporators and an early manager of the Philadelphia Savings Fund Society. He helped to establish the House of Refuge. In 1834, he became Professor of Moral Philosophy, English Literature, and Chemistry at Haverford College. He returned to Philadelphia twelve years later and re-entered business. He became the first President of the American Pharmaceutical Association in 1852. In 1853, he retired from business and lived in Germantown until his decease in 1883.

ROBERT MILNOR was a druggist at 161 South Second Street. He was long connected with the College and continued as a member until 1841 without ever taking an active part, so far as the records show.

PETER WILLIAMSON was a youth of 24 in 1821. He was the presiding officer at the semi-centennial in 1851. He was

connected with the establishment of many charitable and philanthropic organizations and was later grand master of Free and Accepted Masons in Pennsylvania. He established the first free scholarship for tuition in the Philadelphia College of Pharmacy, was the Founder of the Southwark Dispensary and a Warden in the Episcopal Church in Southwark.

STEPHEN NORTH was a wholesale druggist at 14 North Second Street, of whom we know but little, as he was evidently but a young man and died in 1826, but a few years later. He was second Vice-President of the College from 1821 to 1824, and first Vice-President from 1824 until his decease.

HENRY TROTH was a young man of 27 when the Carpenters' Hall meeting was held. He learned the drug business with Jeremiah Morris in the store on Market Street, near Seventh. He aided in the establishment of the Philadelphia Literary Association, afterward including a noteworthy group of men prominent in civic and educational affairs. In 1815, when he was but 20 years of age, he formed a partnership with his brother-in-law, Edward Needles, another druggist, under the name of Henry Troth & Co., wholesale druggists. He was one of the originators of the House of Refuge, a manager of the Schuylkill Navigation Company, and was connected prominently with many other philanthropic, business and scientific organizations. He was a member of the Philadelphia Councils for nine years, part of which time he presided over that body. He was a trustee of Girard College, and a Director of the Bank of the United States. He was one of the first to burn anthracite coal in a grate and he was one of those who urged and aided in the introduction of illuminating gas. Besides being one of the founders of the Philadelphia College of Pharmacy, he was its Vice-President for 13 years, and presided over many of its meetings. He was chairman of its Board of Trustees for many years, and died in 1892.

SAMUEL BIDDLE was a druggist of 142 High Street, concerning whom we know little, as he, too, died a few years after, in 1824.

CHARLES ALLEN was a druggist at 160 South Second Street, resigned in 1827 and removed from the city.

FREDERICK BROWN was another young man of 25, who learned the drug business with Charles Marshall, beginning with 1812, and was associated with him for a number of years subsequently. He was in business for himself at Fifth and Chestnut Streets for many years. He, too, was prominently identified with the development and work of many Philadelphia institutions, was manager of the Pennsylvania Hospital for a time, and one of the founders of Laurel Hill Cemetery.

These brief sketches show the type of men who founded this great Institution. It was an enterprise of youth, for the average age of the five whose ages we know, was but 28 years at the time of the founding, the oldest being Samuel Jackson, who was 34, and the youngest, Peter Williamson, who was but 24.

We owe a debt of gratitude, too, for the selection of Carpenters' Hall for their initial meeting. It is in harmony with the high ideals subsequently displayed in handling the affairs of the College.

This Committee called their associates together on March 13th, at which time they recommended the establishment of a College of Apothecaries and the erection of a School of Pharmacy. There were sixty-eight charter members of this proposed college. Their names and addresses at that time are as follows:

Charles Marshall	56 Chestnut Street
Jeremiah Morris	293 High (Market) Street
William Heyl	35 High Street
John Elliott	60 South Front Street
Peter Lehman	320 High Street
Daniel Elliott	60 South Front Street
Wm. Revoudt, M.D.	Wood Street and Old York Road
Mathias Pleis	461 North 2nd Street
Edmund Pryor	373 North Front Street
Thomas Wiltberger	169 North 2nd Street
Jacob Bigonet	158 Lombard Street
Frederick Klett	261 North 2nd Street
Thomas Cave	298 High Street
Caleb Ash, Jr.	66 North 9th Street

Thomas A. Mason	183 South 6th Street
Alexander Fullerton, Jr.	33 Filbert Street.
Edward Needles	222 High Street
Charles Thomson	34 Sassafras (Race) Street
George Glentworth	Chester and Race Streets
Daniel Thatcher	2nd and High Streets
Thomas Evans	3rd and Spruce Streets
Anthony H. Morris	45 North 3rd Street
Jeremiah Emlen	6 North 3rd Street
William Lehman	76 South 2nd Street
Stephen North	14 North 2nd Street
Charles Allen	160 South 2nd Street
Warder Morris	45 North 3rd Street
Edward B. Garrigues	6 North 6th Street
Robert Milnor	162 South 2nd Street
James W. Simes	459 High Street
James S. Ewing	221 Chestnut Street
George D. Wetherill	16 Arch Street
Isaac Thomson	2nd and High Streets
James L. Smith	134 Chestnut Street
Anthony Ecky	83 Union Street
Charles Ellis	56 Chestnut Street
Mordecai L. Gordon	66 North 2nd Street
Algernon S. Roberts	76 South 2nd Street
John P. Wetherill	65 North Front Street
Daniel Laws	5th and Spruce Streets
Edward Lowber	144 North 3rd Street
Charles Yarnall	24 North Front Street
Henry M. Zollickoffer	6th and Pine Streets
Samuel Biddle	142 High Street
Charles Treichel	99 Walnut Street
Daniel B. Smith	33 High Street
Charles Marshall, Jr.	310 High Street
Samuel Jackson, M.D.	40 North 4th Street
Henry Troth	222 High Street
Thomas McClintock	107 South 9th Street
Elisha Crowell	2nd and Shippen Streets
Samuel P. Wetherill	65 North Front Street
William Baker	6 North 5th Street
Joseph Allen	202 South 3rd Street

Peter Williamson	2nd and Almond Streets
William C. Poole	62 North 2nd Street
Richard Jordan	3rd and Coates Streets
Frederick Brown	56 Chestnut Street
Thomas Oliver	Front and Catharine Streets
George H. Burgin, M.D.	55½ North 3rd Street
Solomon Temple	121 High Street
Eleazer L. Cohen	239 Market Street
John J. Smith, Jr.	121 High Street
Charles Wetherill	65 North Front Street
George Babe	Front and Cedar Streets
Charles Rizer	5th and Passyunk Avenue
Wilson Jewell, M.D.	
Peter Thomson, Jr.	

These charter members, by their support and guidance, likewise deserve credit in the founding of the College, for from their ranks came the officers and workers of many subsequent years of activity, and among them were individuals of great prominence in city affairs later.

On March 27th, 1821, scarcely five weeks after the initial meeting on February 23rd, the Philadelphia College of Apothecaries was duly organized with the following officers, concerning each of whom a monograph might be written if space and time afforded.

Charles Marshall, President  
William Lehman, First Vice-President  
Stephen North, Second Vice-President  
William Heyl, Treasurer  
Daniel B. Smith, Secretary

#### MEMBERS OF THE BOARD OF TRUSTEES

Charles Allen	Henry M. Zollickoffer
Samuel Biddle	Samuel P. Wetherill
Daniel Thatcher	Warder Morris
Samuel Jackson	Daniel Elliott
Peter Williamson	Jeremiah Morris
Charles Marshall, Jr.	Henry Troth
Peter Lehman	Thomas Wiltberger
Thomas McClintock	Frederick Brown

The Trustees promptly met and organized by drafting by-laws, appointing committees, etc., and the committee appointed for that purpose reported on plans for instruction.

Early in April, Samuel Jackson, M.D., was elected Professor of Materia Medica and Pharmacy, and Gerard Troost, M.D., was elected Professor of Chemistry.

Samuel Jackson's career has already been described. Of that of Gerard Troost much might be written. He was a native of Holland who had but recently settled in America, who, during the few years he resided in Philadelphia, identified himself with much that was important in its scientific development. He was the first President of the Academy of Natural Sciences, later removed to Nashville, where he associated himself with the State University, and still later, becoming State Geologist, made an illustrious name for himself as paleontologist.

These original professors were the first of an illustrious line, of which not only our Institution but American Pharmacy and American Medicine may be justly proud. During the first half century of the College, the following names are those of professors of pharmacy, materia medica and chemistry: Jackson, Troost, Ellis, Wood, Bache Griffith, Fisher, Bridges, Carson, Thomas, Parrish and Procter.

In addition to inaugurating the course of instruction which was planned to start the following November the members of the College established rules and regulations for the conduct of the business on the part of the members of the College, which later developed into the earliest code of pharmaceutical ethics established in America.

It is interesting to observe from newspaper advertisements published shortly before the course of lectures started how explicitly all of the details are discussed and how frankly the reasons for founding the College are stated.

From Poulson's *American Daily Advertiser*, Monday, October 29, 1821:

"COLLEGE OF APOTHECARIES.

"In the division of the sciences that characterizes the philosophy of the present age, and which has so much tended to their improvement, Pharmacy has been withdrawn from the charge of the Physician, and consigned to the care of the Apothecary. In Europe, this division has long been recognized and sanctioned by the Medical Profession. Colleges of Apothecaries, and other similar institutions, have been established, devoted expressly to instruc-



tion in Pharmacy and its subsidiary sciences. On the continent, most of the respective governments have prohibited, under heavy penalties, any one from selling or preparing Drugs and Medicines for administration, who has not passed through a course of instruction, and become practically acquainted with the business. In Great Britain, most Apothecaries are regularly instructed, by attendance on the lectures of the Colleges of Apothecaries of London and Dublin, and are associated as members, while abuses in the business are guarded against by severe penalties, enacted by Parliamentary statute.

"In this country, Pharmacy has been entirely neglected, as a science. Previous instruction has not been considered indispensable, in order to capacitate an Apothecary for pursuing his profession, while very few practitioners of Medicine possessed more than a superficial acquaintance with the principles and details of Pharmaceutic knowledge. From this state of things, many evils, some of a serious and aggravated nature, have flowed, urgently requiring correction.

"Many Apothecaries of this city, have long been sensible of the necessity of taking some efficient measures, by which the irregularities and abuses that have crept into their business, should be abolished; and that their profession should be placed on that respectable footing to which it is entitled, by its usefulness to society, and as an important branch of the science of Medicine. With these views, they have founded the PHILADELPHIA COLLEGE OF APOTHECARIES.

"This institution has already established many wholesome regulations for the government of its members, calculated to inspire confidence in all those who are attached to it; and has provided for a course of public instruction, under its auspices, in *Materia Medica* and Pharmacy, and Pharmaceutic Chemistry, with the intention of adding, ultimately, other collateral sciences. A Cabinet is also forming of choice and selected specimens of Drugs and Medicines, of the best qualities.

"An institution embracing so many subjects of high importance and utility to the Medical Profession, and the public generally, and so well calculated to perfect those objects, cannot fail to meet the approbation and support of the liberal and well-informed practitioner, and every member of society.

"The College announces, that the Courses of Lectures will commence in the first week in November, and will be delivered three times a week, in the evening, during the winter, in the Hall of the German Society, South Seventh Street.

"Lectures on *Materia Medica* and Pharmacy, by Dr. Samuel Jackson.

"Lectures on Pharmaceutic Chemistry, by Dr. Gerard Troost.

"By order of the Board of Trustees.

"PETER WILLIAMSON,

*"Secretary."*

From Poulson's *Daily Advertiser*, Tuesday morning, November 6, 1821:

## "PHILADELPHIA COLLEGE OF APOTHECARIES.

"The Introductory Lecture to the course on *Materia Medica* and Pharmacy, will be delivered by Samuel Jackson, M.D., on Friday evening, November 9th, in the German Society's Hall, in South Seventh Street, between Market and Chestnut; and

"The Introductory Lecture, to the course of Pharmaceutic Chemistry, will be delivered by Gerard Troost, M.D., on Saturday evening, November 10th, at the same time and place."

In the following year, 1822, when the College was incorporated, the name was changed from the "Philadelphia College of Apothecaries" to "The Philadelphia College of Pharmacy." This advertisement of several years later will also be found to be of interest.

From the *National Gazette and Literary Register*, Philadelphia, Saturday afternoon, November 13, 1824:

## "PHILADELPHIA COLLEGE OF PHARMACY.

"The Lectures in this Institution will commence about the middle of the ensuing month (November), at the Hall occupied by the College, in Seventh Street below Market.

"The Course on *Materia Medica* and Pharmacy will be delivered by Samuel Jackson, M.D. It will embrace a concise History of the Articles used in, or connected with Medicine; and an exposition of their sensible and medical qualities; their various official preparations, and the modes of detecting spurious, or sophisticated varieties.

"The course on Chemistry, will be delivered by George B. Wood, M.D., and will, in addition to the application of this science, to Pharmacy, comprehend a complete series of popular Lectures on Chemistry, illustrated by numerous Experiments, with an extensive Apparatus.

"There is belonging to the College, a large collection of superior Specimens of the various articles comprised in the *Materia Medica*, which will be exhibited by the Professors to their classes, and are well calculated to add to the interest and instruction of the Lectures.

"Tickets of Admission to be had of William Heyl, Treasurer, No. 215 Market Street, or Daniel B. Smith, Secretary to the College, corner of Arch and Sixth Streets, Price \$5.00 each course, and a matriculating fee of \$2.00 to be paid by all except apprentices to members of the College.

"By order of the Board of Trustees.

"HENRY TROTH, *Chairman*;

"WILLIAM BAKER, *Secretary*."

The apparent discord or opposition between the University of Pennsylvania and the Founders of the College has occasionally been magnified and distorted by those unfamiliar with the facts as indicating a long continued and bitter enmity between the University of Pennsylvania and the Philadelphia College of Pharmacy.

Nothing could be further from the truth. It is a matter of record that the University of Pennsylvania, in partial pursuance of its original plan did confer the degree of Master of Pharmacy as an honorary degree upon sixteen Philadelphia Apothecaries in April, 1821. It is illuminating to note that of these sixteen who were so honored, seven were charter members of the newly formed College.

It is also of interest to learn that very soon after the active functioning of the College began, when the members showed the breadth of their aims by conferring honorary membership upon such international authorities as Paris, Chapman, Silliman, Vauquelin, Derosne, Robiquet, Virey, Pelletier, Faraday, Torrey, Nuttall, Brandes, Doberciner and Trommsdorff, that there was also included the name of Dr. John Redman Coxe, who is credited in the memoirs of Edward Parrish as having been the leading spirit in the original movement by the University of Pennsylvania.

Of interest in this same connection, too, are the tributes of some of the University's own teachers.

In the "Early History of the University of Pennsylvania," written by Dr. George B. Wood in 1834, he states:

"The degree of Master of Pharmacy was instituted a few years since with the very laudable view of improving the profession of the apothecary, which, in the city, has assumed an importance far beyond what it possesses in other parts of the United States. Any person is entitled to the degree who shall have served an apprenticeship of at least three years with a respectable apothecary, and attended two courses of lectures on Chemistry and Materia Medica in the University. Advantages would no doubt have accrued from this accession to the original plan of the medical department had it not been superseded by the establishment by the apothecaries themselves of a distinct school, which being under their own management, and directed to the one object of advancing the usefulness and respectability of the profession, is naturally more popular, and at least equally efficient."

Later, Dr. Joseph Carson, in his "History of the University of Pennsylvania," published in 1859, says:

"This procedure on the part of the University, in the matter of improving and elevating the practice of pharmacy, aroused the enterprising spirit of the druggists and apothecaries of Philadelphia, and incited them to found the College of Pharmacy, an independent institution, which, through the instrumentality of its school, and of its journal, and by its vigilance with reference to the conduct of its members, has been of incalculable service to the profession of pharmacy, not only in the city of Philadelphia, but throughout the United States."

And now in our own time comes this congratulatory tribute from the one who has guided the destinies of the University of Pennsylvania for the preceding decade and who has been associated with its work for more than thirty years:

"The 100th birthday of the College of Pharmacy is now here. My congratulations are herewith extended to the College and its many children. It is pleasant to recall that from its beginning the University of Pennsylvania and the College have sustained the most cordial relations. Sons of the University and many of its professors worked in the ranks of the College.

"I think it is conceded that this harmonious co-operation has redounded to the good of each institution. The eminent Botanists and Chemists of the two foundations have mutually sustained and encouraged one another in their several efforts to advance the interests of their respective sciences.

"For myself, I can only say that the career of the College of Pharmacy during my intimate knowledge of it has been most inspiring. It has stood for the best in every direction. The glories of its past I shall not dwell upon. Others will do that. Its advancement is surely a joy to its many friends in this city and to the active promoters of science everywhere. I'm certain the University of Pennsylvania joins me in its well wishes for a still more glorious future.

"Rejoicingly and faithfully yours,

"EDGAR F. SMITH."

And now, as the time comes for me to close, with the inspiration which comes from such surroundings and such glorious traditions and records I can think of no more appropriate lines than those of Kipling in his "Fathers of Old," for he has crystallized for all time the thought that is uppermost in our minds and hearts—reverence for the past and inspiration for the future.

#### OUR FATHERS OF OLD.

Excellent herbs had our fathers of old—

Excellent herbs to ease their pain—

Alexanders and Marigold,

Eyebright, Orris and Elecampane,

Basil, Rocket, Valerian, Rue,

(Almost singing themselves they run)

Vervain, Dittany, Call-me-to-you—

Cowslip, Melilot, Rose of the Sun.

Anything green that grew out of the mould

Was an excellent herb to our fathers of old.

Wonderful tales had our fathers of old  
Wonderful tales of the herbs and the stars—  
The Sun was Lord of the Marigold,  
Basil and Rocket belonged to Mars.  
Pat as a sum in division it goes—  
(Every plant had a star bespoke)——  
Who but Venus should govern the Rose?  
Who but Jupiter own the Oak?  
Simply and gravely the facts are told  
In the wonderful books of our fathers of old.

Wonderful little, when all is said,  
Wonderful little our fathers knew.  
Half their remedies cured you dead—  
Most of their teaching was quite untrue.  
“Look at the stars when a patient is ill,  
(Dirt has nothing to do with disease),  
Bleed and blister as much as you will,  
Blister and bleed him as oft as you please.”  
Whence enormous and manifold  
Errors were made by our fathers of old.

Yet when the sickness was sore in the land,  
And neither planets nor herbs assuaged,  
They took their lives in their lancet-hand  
And, oh, what a wonderful war they waged!  
Yes, when the crosses were chalked on the door—  
Yes, when the terrible dead-cart rolled,  
Excellent courage our fathers bore—  
Excellent heart had our fathers of old,  
None too learned, but nobly bold  
Into the fight went our fathers of old.

If it be certain, as Galen says,  
And sage Hippocrates holds as much—  
“That those afflicted by doubts and dismays  
Are mightily helped by a dead man’s touch,”  
Then, be good to us, stars above!  
Then, be good to us, herbs below!  
We are afflicted by what we can prove,  
We are distracted by what we know.  
So—ah, so!  
Down from your heaven or up from your mould,  
Send us the hearts of our fathers of old!

## PHARMACY, 100 YEARS AGO.\*

By H. V. ARNY, Ph.G. (1889); Ph.M. (1919).

## INTRODUCTION.

All hail! Alma Mater, upon this thy Centennial! Permit one of thy children in the midst of this distinguished assemblage of thy sons and thy daughters to offer a tribute of affection, of esteem and of gratitude. For a century, those entrusted with thy affairs have maintained a great ideal; the conducting of a college of pharmacists, for pharmacists by pharmacists. May this ideal, successfully maintained for one hundred years, actuate thy disciples during the hundreds of years to come.

## AMERICA, 100 YEARS AGO.

Eighteen Twenty-One, the year that James Monroe began his second presidential term, the Era of Good Feeling, after an election in which he secured all of the electoral votes save one; the term that brought into being the Monroe Doctrine (1823).

Eighteen Twenty-One, when John Quincy Adams was Secretary of State, the very year he issued his Report on Weights and Measures, in some respects the most remarkable dissertation on metrology ever written.

Eighteen Twenty-One, when John Marshall was Chief Justice of the Supreme Court and was clarifying the Constitution by his illuminating decisions.

Eighteen Twenty-One, when John Adams and Thomas Jefferson were living in distinguished retirement awaiting the Final Summons, which, when it came to both of them upon the Semi-Centennial of the signing of the Declaration of Independence (July 4, 1826), created the most interesting coincidence in American history.

Eighteen Twenty-One, when Philadelphia was the largest city in the United States, a thriving place of over 137,000 inhabitants; when New York ranked second, with over 123,000 inhabitants; when New Orleans, the delightful city depicted in Cable's *Grandis-simes*, had over 40,000 inhabitants; when Cincinnati was a recently

\*An address delivered at the Centennial Celebration of Founders' Day, February 23, 1921.

incorporated city of 10,000 inhabitants; when Cleveland was a frontier post of 500 souls; when Chicago was merely a few shacks around Fort Dearborn; when San Francisco was "a vast solitude" as found by Dana in 1835, with its Presidio six miles from the landing place of occasional ships and with its nearest mission four miles away.

Eighteen Twenty-One, when it took two days and a good part of one night, by stage and boat and a night of rest en route, to travel from New York to Washington; and when the "Fast Post Coach" from New York to Philadelphia meant taking a steam ferry at the former city at 6 A. M., riding over to Elizabethtown, and from thence across New Jersey and down the Delaware to Philadelphia, which was reached at 4 P. M.; when steamboat traffic was only fourteen years old; when the Erie Canal (a marvel in those days) was being constructed; when the only railroad in America was a short gravel-carrying concern near Boston; when the first passenger railroad in America (Baltimore & Ohio, 1829) was merely dreamed of; when illuminating gas was merely an experiment in private establishments, such as the Gas Light Tavern, Second and Walnut, Philadelphia, some years before the New York Gas Company (1823) and the Philadelphia Corporation (1836) obtained their franchises.

Eighteen Twenty-One, when Washington Irving, aged 38 years, was sojourning abroad after the successful publication of "The Sketch Book"; when George Bancroft, just back from the famous Georgia Augusta University in Göttingen (the first American to win a Ph.D degree from that institution), had started in as tutor in Greek at Harvard; when Cooper had just published his first novels, the now forgotten "Precaution" and the still famous "The Spy"; when the youngster Poe was at school in Baltimore; when Longfellow, a lad of 14, entered Bowdoin College, after the publication of his first poem (1820); when another boy of 14, Whittier, was attending district school in New England and had been introduced to the beauties of poetry by his teacher, Joshua Coffin, through the medium of a volume of Burns; when Emerson had just graduated from Harvard.

Eighteen Twenty-One, when Daniel Webster was at the beginning of his brilliant career, the orator of the two hundredth anniversary of the Landing of the Pilgrims; when Henry Clay had temporarily stepped out of the speakership of the House of Repre-

sentatives after successfully getting through the Missouri Compromise (1820); when John C. Calhoun was Secretary of War; when DeWitt Clinton was Governor of New York and was directing the construction of the Erie Canal; when Lincoln, Lee and Jefferson Davis were lads of from 12 to 14, unconscious of their future rôle in the sombre drama of 1861-65; when John Jacob Astor and Peter Cooper were amassing those fortunes that were to bring into being the Cooper Institute and the Astor Library.

Eighteen Twenty-One, when Audubon was gathering material for his great work, "The Birds of North America" (published in 1827); when Nuttall, the Anglo-American botanist and erstwhile Philadelphian, published his book, "Travels in Arkansas in 1819"; when Benjamin Silliman, founder of the *American Journal of Science* (1818), was professor of chemistry, *pharmacy*, geology and mineralogy at Yale College.

#### PHILADELPHIA IN 1821.

As mentioned above, in 1821 Philadelphia was the first city of America in population, and a glimpse of the City of Brotherly Love a century since may be worth while. As to topography, it is interesting to note that Southwark seemed to be the southern edge of the city, while we read that in 1826, when Edward Needles started his store at Twelfth and Race, he was called "the frontier apothecary," since across the street as a large field enclosed in a post and rail fence; that in 1829, Wm. Biddle opened a store at Eleventh and Arch Streets, and feared he was making a mistake in going so far into the suburbs; that in 1821, Farr & Kunzi built their new factory at Ninth and Brown, then the outskirts of the city, and that for years after D. B. Smith opened his store at Sixth and Arch, the neighbors took chairs out into the street and sat under the shade of the trees, all of the morning, without being disturbed by a passing vehicle. In appearance it evidently still resembled the quaint town of 1795, so charmingly described by S. Weir Mitchell in his "Red City"—"the single spire of Christ Church rising high over the red brick city \* \* \* the town stretching north and south along the Delaware, and beyond it the woodland \* \* \* Westward on Chestnut Street, pastures, cows, country, and to the north a fine forest known as the Governor's Wood. \* \* \* A mile further \* \* \* a river flowing slowly by." A town where chains were still put across the streets in front of



the four score of churches during service time, to prevent traffic from interfering with worship.

Considering that a city is what its inhabitants make it, a mention of some of its leaders may be in order. There were the four Biddles, Nicholas, the financier; Clement C., the lawyer; James, the naval officer; and Richard, the writer. Nicholas, then a man of 35 years, within two years of his selection as president of the United States Bank, which made him America's foremost financier, until the unfortunate quarrel between President Jackson and the bank officials in 1836. Then there were Stephen Girard, the business man of Philadelphia and New Orleans, who in 1821, was 61 years old, and William Bartram, the famous son of the famous John, still living at the advanced age of 81. Dr. Caspari Wister, the founder of the famous Wister Parties, had been dead three years; Benjamin West, the first American artist, had died in London the year before (1820); while Edwin Forrest, a boy of 14, had already made (1820) his theatrical debut as Douglas in a popular play of that time.

Scientific Philadelphia was as much in the fore then as it had been in the days of Franklin, Rittenhouse and Bartram, and as it is today. The University of Pennsylvania was then in its first flower, and among its faculty of 1821 we note Dr. Robert Hare elected professor of chemistry in 1818, the great experimenter, the inventor of the oxy-hydrogen blow pipe, the great thinker, who, in the light of a disparaging remark made in a certain one of his obituary notices, may have been a century ahead of his time as far as psychic phenomena are concerned; Dr. John Redmond Coxe, professor of *Materia Medica* (1818-1835), known to all of us as the author of Coxe's American Dispensatory and curiously embalmed in the literature of pharmacy as the deviser of Coxe's hive syrup; Dr. George B. Wood, lecturer in medical chemistry, destined to become the second professor of chemistry at the Philadelphia College of Pharmacy (1822-1831), and one of the founders of "the druggists' Bible," the United States Dispensatory; and Dr. Samuel Jackson, professor of the institutes of medicine (in 1835), first professor of *Materia Medica* at the Philadelphia College of Pharmacy (1821-1827), author of "Principles of Medicine" (1838), deviser of Jackson's pectoral syrup, eminent physician, whose intimacy with the French pharmacist, Durand, caused many heart burnings among the other druggists of the period. Among the

other scientists of Philadelphia in 1821 were Dr. Franklin Bache, who in 1819, at the age of 27, published his "System of Chemistry," who was chosen as professor of chemistry at Franklin Institute upon its organization (1826), who was professor of chemistry at the Philadelphia College of Pharmacy from 1831 to 1841, who was Dr. Wood's associate in founding the United States Dispensatory, and who was professor of chemistry at Jefferson Medical College from 1841 until his death in 1864. Then there was Dr. Gerard Troost, who, we glean from the scanty material at our disposal, was manufacturing ferrous salts at Cape Sable, Md., in 1817, who had a chemical factory in Philadelphia in 1820, who was professor of chemistry at the Philadelphia College of Pharmacy during the first year of its existence, and who a few years later moved to Tennessee, where he became one of the founders of the University of Nashville.

#### PHARMACEUTICAL AMERICA IN 1821.

Very elusive is the biographical data concerning the druggists of a century ago. The first American pharmaceutical publication, the venerable JOURNAL of this college, which has taken a new lease on life under the editorship of Mr. Beringer, did not appear until 1825, and the first volume includes eight fascicles published between that date and 1830. Of the Founders whom we are here gathered to honor, there are three of whom no biographical record has been found. As to the others, from obituaries and from other sources, we glean the following information:

HENRY TROTH: "The Founder of the Philadelphia College of Pharmacy," as Profesor Remington has called him, had in 1821, a wholesale drug store at Seventh and Market. A capable and progressive man he was, one of the first Philadelphians to burn anthracite coal (which cost \$8.40 a ton in 1818), in his open grate; one of the members of the Common Council, from 1827 to 1836, making a vigorous fight for the granting of a gas franchise from 1833 to 1836.

PETER K. LEHMAN, whose conversation with Mr. Troth as to the proposition of the granting of the Master of Pharmacy degree by the University led to the historic meeting at Carpenters' Hall a century since, had, in 1821, a drug store at Tenth and Market Streets.

CHARLES MARSHALL, the first President of the Philadelphia College of Pharmacy, descendant of a distinguished line of Philadelphia apothecaries, in 1821, had a drug store at 56 Chestnut Street, which he, a man of 77 years, conducted with the help of his remarkable daughter, Elizabeth, who when her father lost his first modest fortune in 1804, encouraged him to start anew with the front room of their house converted into a little shop, which by 1821 had grown into a highly prosperous establishment.

WILLIAM LEHMAN, elected first Vice-President at the Philadelphia College of Pharmacy organization meeting, had a drug store on Second Street, between Arch and Race. He was a member of the Legislature from 1814 until his death in 1829, when he willed \$10,000, a considerable sum in those days, to the Philadelphia Athenæum, inaugurating a custom, followed by too many wealthy pharmacists since that time, of bestowing their largess upon worthy objects outside of the institutions of their own calling.

STEPHEN NORTH was chairman of the Carpenters' Hall meeting and was elected Second Vice-President at the organization meeting of the Philadelphia College of Pharmacy. All that has come to light concerning him is that he was a wholesale druggist and that he died in 1826.

PETER WILLIAMSON, the secretary of the Carpenters' Hall meeting, in 1821, was a partner in the drug store of Klapp & Williamson, Second and Almond Streets. In 1874 he founded the Peter Williamson scholarship, which has been of great service to many young men since. He died in 1886 at the advanced age of 91 years.

DANIEL B. SMITH, the first Secretary of the Philadelphia College of Pharmacy, in 1821, was a partner in the firm of Smith & Hodgson, Sixth and Arch, a store that eventually developed into the business of Bullock and Crenshaw. Mr. Smith is one of the numerous illustrations of the scholar in pharmacy that gives the lie to the flippant opinion handed down in 1912 from the Federal Bench in New York, in which occurred the phrase "druggists all over the country: men of no great learning." Besides his activity in the Philadelphia College of Pharmacy, he became, in 1834, professor of philosophy, literature and chemistry at Haverford College.

FREDERICK BROWN, one of the Founders, in 1821, was a drug clerk, employed by Charles Marshall. In 1822, he started his own successful business, which he continued until his death in 1864.

Among the other Philadelphia druggists of 1821 and shortly thereafter we note the following:

BENJAMIN ELLIS, originally a druggist at Muncy, Pa., in 1821, was studying medicine at the University of Pennsylvania. In 1827, he became professor of materia medica at the Philadelphia College of Pharmacy.

FRANKLIN SMITH, in 1821 or shortly thereafter, had a drug store at Eighth and Walnut. He was the preceptor of Henry C. Blair, who in 1828, bought the Smith drug store and thus established the historic Blair pharmacies.

GEORGE GLENTWORTH, in 1821, conducted, at Sassafras (now Race) and Chester Streets, the pharmacy, the fixtures of which are now exhibited in the College Museum.

ELIAS DURAND, in 1821, was a clerk in Ducatel's famous French pharmacy in Baltimore. In 1825, he opened his pharmacy at Sixth and Chestnut, Philadelphia, which for many years was the most renowned drug store in the city. He was vice-president of the Philadelphia College of Pharmacy in 1844 and contributed numerous papers to the JOURNAL.

As to pharmacy in Boston in 1821, a delightful series of thirteen papers by W. A. Brewer that appeared in the *Pharmaceutical Record* in 1884, gives the most vivid picture of the time that has as yet been found. The series tempts one to make numerous quotations, but at this time it can only be stated that Mr. Brewer began his pharmaceutical apprenticeship in June, 1821, in the wholesale drug store of Bartlett and Brewer on Washington (then Cornwall) Street, Boston. He states that at that time the wholesale firm of Rice, Henshaw & Company was the largest drug distributors in the United States; that David Henshaw later became Secretary of the Navy; that in 1821, there were in Boston seven wholesale and twenty-three retail drug stores, among these being those of George Brinley, Robert Fennelly, Charles Nolan, John I. Brown (of bronchial troches fame), Maynard and Noyes, Love and Reed;

Dr. Ballard, Cyrus Holbrook, Charles White, Ephraim Elliot and Thomas Greenleaf.

As to the New York druggists in 1821, those whom we still recall are Schiefelin & Company, then a firm of twenty-seven years standing; John Milhau, who in 1823, retired, spent several years abroad and then returned to open the famous Milhau Pharmacy on Broadway; and Benjamin, Quackinbush, Greenwich and West Tenth, whose store is still run by his descendants. From the city directory of 1821 and from other sources we learn that among the other New York apothecaries of that time were Peter B. Brown, Grand and Cannon Streets; Hull and Bowne, 146 Pearl Street; J. H. & W. B. Post, 41 William Street; James Seaman & Company, 49 Fulton Street; and Isaac See, 325 Greenwich Street.

For information as to the druggists of Cincinnati of 1821 we are indebted to an interesting historical sketch by Joseph Feil, in which are given from the newspapers of 1818 and 1819 advertisements of T. W. Dyott, wholesale drug and medicine warehouse; Caleb Bates, Lower Market Street; and Hallam & Clark. Of the other American cities the information is only fragmentary. Thus we learn from obituaries and from patent medicine advertisements that Ducatel's pharmacy was one of the leading drug stores of Baltimore; that William Gunton was established in Washington; that E. & R. H. Stabler conducted the drug store in Alexandria, from which sprang R. H. Stabler, the eighteenth president of the American Pharmaceutical Association; that William McKean was established in New Orleans.

As to the actual drug business of 1821, we have a mirror of its materia medica in the United States Pharmacopœia of 1820. The druggist made almost all of the medicines that he dispensed. Thus the U. S. P. 1820 provided recipes for such chemicals as prussic acid, sulphuric ether, silver nitrate, bismuth subnitrate, calomel, corrosive sublimate and zinc oxide (flowers of zinc), and record shows that independent chemical works were just in the process of organization (*e. g.* Farr and Kunzi, 1818; Rosengarten & Zeitler, 1822). All pharmaceuticals were prepared by the apothecary except some special ones, mainly of French origin, as at that time the French were the premier pharmacists of the world. Testimony to this effect is given by D. B. Smith concerning Charles Marshall, while it can be added that the tremendous vogue of Elias Durand was due to the fact that he was a French-trained pharma-

cist and could prepare pharmaceuticals of an elegance almost equalling that of the French preparations. In a curiously fragmentary contribution from S. F. Troth, he brings out that the first really nice Epsom Salt was brought from England to Philadelphia in 1821; that the first sodium bicarbonate purchased by Henry Troth, in 1821, cost \$1.25 a pound; that tartaric acid was a novelty in 1821, and cost \$1.25 a pound; and that about that time druggists had their English magnesium carbonate calcined to the oxide in the furnaces at Adam Miller's pottery on Zane Street. From an advertisement of a Cincinnati druggist we learn that in 1819, beeswax cost 20 cents a pound; cassia, 70 cents; ginger, 30 cents; and sugar, 28 cents. Another Cincinnati advertisement of 1819 announces the receipt from Philadelphia of a consignment of Milnor's Acid Lemon for making lemonade, and of Farr's Soda Powder for making soda water. In passing it might be stated that the first American quinine was made in 1823 by Farr and Kunzi, the firm that eventually developed into the Powers and Weightman factory.

#### PHARMACEUTICAL THOUGHT IN 1821.

To discuss the general trend of science in 1821 would exceed the limits of this paper, so there is no need of going further in this direction than to cite what Edward Parrish said fifty years ago today, to that effect that in 1821 the labors of Davy, Ampere, Dalton, Berzelius, Faraday, Oerstedt and Arago had reached their culmination, thus laying the foundations of modern chemistry.

William Procter pointed out the difficulty in making a history of pharmacy of the 1821 period, since the only pharmaceutical journals then reaching this country were French. It has been the privilege of the writer of this paper to scan the *Journal de Pharmacie* for 1821, and also two German year books of pharmacy of the same period, Kastner's *Berlinische Jahrbuch* and the *Scheidekünstler und Apotheker Almanach*. From these sources considerable interesting information has been obtained; among it the fact that in France, the available journals of science, besides the *Journal de Pharmacie*, numbered seventy. Of these only one was pharmaceutical (Trommsdorff's *Journal der Chemie und Pharmazie*) and only one came from America (*Journal of the Philadelphia Academy of Sciences*). In the two German Year Books are lists of books and periodicals received by the editors during the

year. Among the periodicals we note Trommsdorff's *Journal der Pharmazie* and Buchner's *Repertorium*. As to books, over eighty titles are given.

Turning to the problems under discussion it is plain to see that 1820-1821 were alkaloidal years. Sertürner's discovery of morphine, the first isolated plant base (1816), had stimulated research in that direction and as a result we find in the periodicals of a century ago, first of all, the classic paper of Pelletier and Caventou on quinine, a dissertation covering forty-eight printed pages; a paper from the same authors on veratrine, and one from them on strychnine; Meissner's article on sabadilline; Brandes on daturine, on delphine and delphinine and on atropine; Pelletier on veratrine; Oerstedt (son of a Danish apothecary, the great electrician and chemist), on piperine; Desfosses on solanine; Thomsen on the combustion assay of morphine, and Brandt and Meissner on atropine. As novelties in the way of elements we note cadmium, thorium, lithium and selenium. As new drugs, are described *Asarum Canadensis* (used then in the United States for tetanus) guarana, arrow-root, *scutellaria* (used then in the United States for hydrophobia *lactucarium*, Borneo camphor, *chiretta* and *pareira brava*. Then there are given, among other analysis, that of *krameria* by Gmelin; of *ambergris* by Pelletier and Caventou; of Tonquin musk by Blondeau and Guibourt; of *cubeb* by Pelletier; of *Fucus vesiculosus* by Coindet (pointing out that its medical action in goiter is due to its iodine content); of *serpentaria* by Chevallier; of saffron by Henry (noting presence of polychroit); of *santonica* by Boullon-LaGrange (describing its volatile oil); of cochineal by Pelletier and Caventou (giving method of preparing carmine; of yellow wax by Buchholz and Brandes; of *colocynth* and star anise by Meissner; of myrrh by Brandes; and of saffron by Aschoff. An unexpected paper is one on the "Atech-Gab" of Baku, in which the words "petrol" and "napthe" are used, and in which it is stated that the "petrol" is used by the poorer classes of Persians as a lamp oil. Some forty years later (1859) Pennsylvania petroleum became the great commodity which has made it world-famous ever since.

Of papers published by Americans we find four; one by Spalding (the *scutellaria* article cited above), one by Hare on a theory of galvanism, one by Rafinesque on atmospheric dust, and one by

John Gorham, professor of chemistry at Harvard, on the constituents of maize.

There are some unusual items, including a complaint concerning a blind prescription written by a Parisian oculist which could be compounded at only one pharmacy. The prescription called for 6 grains of "purified salt of cadium" in 6 ounces of orange flower water. Because of the extreme rarity of the cadmium compound, the pharmacist charged 4 francs 50 and then, alas, dispensed 6 grains of zinc sulphate. So some of our pharmaceutical predecessors were not so guileless, after all. Another writer rails against factory-made pharmaceuticals, pointing out that one firm sold Baume Tranquille (infused oil of hyocyamus) for 1 franc 20 a pound, whereas the oil of which it was made, when of proper quality cost 1 franc 60. It is also interesting to note that while the metric system was supposedly adopted in France in 1793, thirty years later (1821), practically all matters concerning weight were expressed in pounds, ounces and grains. This should show us metric advocates that it takes a long time to teach a people new ways; it should also show us that patient and persistent effort finally brings a people to the new and better way.

There are two interesting papers which discuss the pharmacists of the past. One calls attention to the fact that the fern genus *Darea* is named after the English pharmacist Dare; in the other mention is made of Apothecary Rouvier as author of a book of voyages; of Apothecary DeMach, as a poet; of Apothecary Guairat as a Latin versifier, and of Apothecary Baumé as the author of a grammar. All of these worthies (all forgotten except Baumé) are discussed in a review of a book on metaphysics published in 1821 by Apothecary Opoix. Here is a good lead for the pharmaceutical historian.

In another paper we find a complaint that works on pharmacy are being written in the vernacular rather than in Latin, a really valid reason for the objection being that when written in the vernacular any charlatan can read the various recipes and thus become druggists, whereas when in Latin, only the truly educated can become apothecaries.

As to books, the first national pharmacopœia, the French Codex, had appeared in 1818, followed toward the end of 1820 by the first United States Pharmacopœia. The great book on pharmacy of the day was by the French pharmacist, Virey, who interestingly



enough had been accused by the Government of appropriating too freely material found in the Codex. At his trial, however, he was acquitted of the charge. The great book for American druggists was Thatcher's American Dispensatory; our present classic, the United States Dispensatory, not appearing until 1833. The most important book on general chemistry was Thomson's System of Chemistry, an English work in four volumes, that was first published in America in 1818. Another classic was Ure's Dictionary of Chemistry, the first American edition of which (edited by Robert Hare and Franklin Bache) appeared in 1821.

The Medical Botany of William P. C. Barton, a handsome volume with beautiful colored illustrations of medicinal plants drawn by the author, appeared first in 1818, with a second edition dated 1825. It is interesting to note the 1818 edition was published by M. Carey & Son, while the 1825 issue was distributed by Carey & Lea, the predecessors of the present firm of Lea & Febiger.

A remarkable book, published around 1821, is a neatly bound volume of 161 pages, extolling the virtues of Swaim's Panacea. After a description of this marvelous concoction by Swaim (a Philadelphia bookbinder), the rest of the volume is taken up with testimonials written up as "reports of cases" from physicians, including such celebrities as Drs. Valentine Mott, Parke (both delegates to the Pharmacopœial Convention of 1820), Dewee and Hall, the latter a member of Congress from North Carolina. There was evidently no Council on Pharmacy and Chemistry in 1821.

#### PHARMACY OF 1821 AND PHARMACY OF 1921.

A comparison between the pharmacy of today and the pharmacy of a century since would constitute a paper in itself, so merely as summary it may be here stated that while pharmacy of 1821 was the art of compounding medicaments and the sale thereof; the retail pharmacy of 1921, the age of the machine-made goods, is largely the art (or science, if you will) of salesmanship, the distribution of the products of other men's hands. Deplore it as we will, the machine has largely replaced the man in our calling as in many others. The druggist of 1821 was a merchant of standing, who served his customers with products made in his back room of his store, and in many cases that back room between now and then has grown into a huge factory. The pharmacist of 1921 has four ways in which he may utilize his training: (a) he may be a

clerk in a corporation drug store; (b) he may be a proprietor of a commercial store, where salesmanship is the keynote, even as it is in the corporation store; (c) he may become a prescription specialist, to whom physicians turn for expert advice, even as the physicians of 1821 turned to Marshall, to Milhau, to Durand and to Ducatel; (d) he may be a trained pharmaceutical chemist or pharamacognosist employed in a manufacturing plant. This is not the time to discuss these phases of modern pharmacy beyond the bare statement that the options may be best expressed by the French saying, *chacun á son goût*.

#### CONCLUSION.

In 1821, the Founders of the Philadelphia College of Pharmacy began this great institution for the purpose of training apprentices to become honest and efficient druggists. It was an organization of pharmacists for pharmacists, and this ideal has been faithfully upheld for one century. It is not improper to say that whatever faults may be found in the century of stewardship have been due to the faithful execution of this principle. Designed originally to train retail pharmacists, as the decades have rolled by, the College has met changing conditions in such a manner that it continues to be of the greatest and broadest service to all phases of American pharmacy. Thus when the time was ripe, laboratory courses of instruction were instituted, courses that brought inspiration as well as knowledge to those who were fortunate enough to take the work. Thus when the old-time apprenticeship system began to break down, when the retail druggist became unmindful of his duty as preceptor, when the commercialization of pharmacy in the modern sense, was at its beginning, the College was the first to start a commercial course that even to this day reflects credit upon its originators. And now at the dawn of the new century of its existence, the Philadelphia College of Pharmacy has become the Philadelphia College of Pharmacy and Science. To its old graduates the College will always remain the beloved "Philadelphia College of Pharmacy," but the new name possesses a striking significance. During the last half-century the university movement in pharmacy has brought about the anomalous condition that its exponents seem at times ashamed that they are pharmacists, and manifest an apparent desire to make pharmacy a minor topic in a course supposedly designed to train a young man or woman to be a pharmacist. It

is on a par with certain phases of medical instruction where the aim seems to teach the student how to diagnose a disease and then let him flounder around as to a remedy. The very title the Philadelphia College of Pharmacy and Science puts the proper emphasis upon the valuation that should be placed upon instruction in this and other schools of pharmacy. Pharmacy should be the foremost consideration. A knowledge of other sciences is essential for the trained pharmacist, but, whether retailer, wholesaler, manufacturer or teacher, the graduates of our pharmacy colleges should realize that they are first, last and at all times, PHARMACISTS.

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## INFLUENCE OF PHARMACISTS ON THE DEVELOPMENT AND ADVANCE OF MODERN CHEMISTRY.\*

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Pharmacy as an art ante-dates modern chemistry by several centuries.

Following the era of the alchemists, and at about the end of the fifteenth century, a different turn was given to the study of alchemy, and under the general influence of Paracelsus, experimentation was turned to the study of new medical qualities in various natural substances, and the projects of transmitting the baser metals into gold and silver were practically abandoned for the time. Paracelsus and his immediate followers made many medical and drug discoveries. Indeed, it has well been said that "the apothecary shops of Europe became research laboratories, from which many valuable medical discoveries emanated."

This was the era of the iatro-chemists. Among these names we have, besides Paracelsus, Libavius, in 1595; Glauber, from 1603 to 1668, whose name still remains a familiar one to the chemist of today, and others.

We are accustomed to think of Priestley, who discovered oxygen, in 1774, as one of the founders of modern chemistry, but

\*An address delivered at the Centennial Celebration of Founders' Day.

Priestly contributed far less to the advance of chemistry than a Swedish apothecary named Scheele, who had discovered oxygen two years before Priestly, although he had not published his discovery until after Priestly's announcement. Scheele also discovered the important element, chlorine, in 1774, and many other of our most important and valuable chemical substances, such as tartaric, oxalic, citric, gallic and lactic acids, as well as glycerin and many other substances. In fact, the work of this Swedish worker, an apothecary during the whole of his career, represents one of the most conspicuous contributions to the advance of chemistry.

If we take one country after another, and look at the records of discovery of the latter part of the eighteenth century, we will find repeated illustrations of the contributions of pharmacists to the stock of chemical knowledge.

For instance, in Germany, Marggraf who, in 1747, discovered beet sugar, and may be said to have been the founder of the beet sugar industry of the world, was a Berlin apothecary, and made many other chemical discoveries. Klaproth, who is credited with the discovery of four of our chemical elements, started as a pharmacist. Heinrich Rose, one of the great mineral chemists, and later Professor in the University of Berlin, began as a pharmacist, and his father and grandfather before him were pharmacists. Poggendorf, Professor of Physics in the University of Berlin, and a name well known in the literature of chemistry, was for eight years a practicing pharmacist.

Turning to the French list, we have the names of Vauquelin, a discoverer of several of our chemical elements, who was connected with the Paris School of Pharmacy, and Pelletier and Caventou, the discoverers of quinine, and Labarraque also actively engaged in pharmacy. The great Pasteur, whose services to chemistry and preventive medicine are universally recognized throughout the world, was an apothecary and not a chemist in the beginning of his career.

Two of the most eminent chemists of our own day, namely, Berthelot and Moissan, were both professors in the *Ecole Supérieure de Pharmacie* in Paris.

Similarly, one of the great lights of English chemistry, in the beginning of the last century, Sir Humphrey Davy, who is credited with the discovery of some seven or eight of our chemical elements, was an apothecary's clerk in the beginning of his career.

Indeed, in both France and England, the recognition of pharmacists as investigators has been notably greater than in any other country. The finest chemical laboratory in London, namely, that of the Imperial College of Science and Technology, had as its first professor of chemistry, one who had the responsibility of constructing the newly established laboratory, the late Sir William Tilden, who began as an apothecary, and for many years was connected with the chemical laboratory of the Pharmaceutical Society of Great Britain. He published, in 1916, a most interesting and valuable book covering the whole range of chemical activity, the title of which is "Chemical Discovery and Invention in the Twentieth Century," which book is one of the most suggestive and readable books to those desiring to get the survey of the broad scope of chemistry and its applications that can be found at the present time.

With this survey of the history of the relations of pharmacists to the development of chemistry in earlier times, as well as in recent times in Europe, we can now come to consider how far this relation has existed in this country.

Speaking in this hall of the Philadelphia College of Pharmacy, and in connection with an anniversary of the founding of this institution, it seems very proper for us to consider what illustration of our subject we may find right here in our past history as an Institution.

Among the most cherished memories of this Institution are those of some of its earliest workers, and in that connection we may call attention to the fine record of one of the earlier professors of this Institution, namely William Procter, Jr., who, though a busy practicing apothecary and a teacher, yet found time to carry on many investigations which advanced chemical knowledge very notably. The value of these was also recognized in much wider circles, and gained for him recognition on the part of foreign chemical authorities. His discovery of the composition of winter-green oil, and of the characters of the salicylic acid derived from the same, were recognized as furnishing the earliest knowledge on this subject.

We may also refer to the long series of contributions to chemical knowledge that have appeared in the AMERICAN JOURNAL OF PHARMACY published by this College for nearly a century past.

✓ Coming down to the present time, we still have very active

workers from the ranks of pharmacy, whose present contribution to chemical science are cordially recognized. While it would be invidious to attempt to select names in this connection, I will only mention two, both of whom are well known to us, namely Professor John U. Lloyd, a recognized authority on plant chemistry, and more recently upon colloid chemistry reactions, and Frederick B. Power, a graduate and former instructor in this College, who is recognized both in England and in this country as probably the first authority upon the subject of essential oils. He is still active in the Government service at Washington on this subject.

The direct influence of pharmacists on the creation of chemical industries is, however, most readily illustrated by a study of the history of the development of manufacturing chemical industries in this city of Philadelphia, which has been known for many years as a great chemical manufacturing center, and I will therefore in some detail review the development of Philadelphia's chemical industries.

"Probably the first to inaugurate the manufacture of chemicals, as such, in this country, was the firm of Christopher, Jr., and Charles Marshall, sons and successors of Christopher Marshall, an early druggist and one of the original 'fighting Quakers' of Philadelphia. This firm had, as early as 1786, entered quite extensively into the business of making muriate of ammonia and Glauber's salt. The factory is described by Watson, in his 'Annals of Philadelphia,' as being a grim and forbidding-looking building on Third Street, near the stone bridge over the Cohocksink Creek. This firm is said to have developed an annual output of upwards of 6000 lbs. of muriate of ammonia; quite an achievement for that time."

Let us now take up the beginnings of the manufacture in Philadelphia of one of the fundamentally important chemicals, viz., sulphuric acid. This substance is recognized as the basis of all chemical industries and its manufacture must precede that of most other chemicals. The theory of the lead-chamber process was already understood by chemists, by the middle of the eighteenth century. Ward had made it in England in 1740 on a large scale in glass vessels, and Dr. Roebuck first used leaden chambers instead of glass in Birmingham in 1746. The first leaden chamber was erected in France, at Rouen, in 1766.

Mr. John Harrison, the son of Thomas Harrison, a member

of the Society of Friends, was an early Philadelphia druggist who had completed his education by spending two years in Europe, in part under the instruction of Dr. Joseph Priestly, the famous English chemist. Upon his return he began, in 1793, the manufacture in Philadelphia of various chemicals, and notably of sulphuric acid. He had at first a lead chamber capable of producing 300 carboys of acid per annum, and his laboratory at this time was on the north side of Green Street, west of Third. In 1804, he established a new factory at Second and Huntingdon Streets, near Frankford Road, Kensington, but continued for a time the work on Green Street. In 1807, he built what was for that time quite a large lead chamber; it was 50 feet long, 18 feet wide, and 18 feet high, and capable of making nearly 500,000 lbs of sulphuric acid annually, the price of which was then as high as 15 cents per lb.

"As is well known, acid produced in lead chambers is not the Oil of Vitriol of commerce, and the only method known at that time to concentrate it to the required strength was by boiling it in glass retorts—a very precarious and dangerous process. The constant breakage of the glass largely increased the cost of the concentrated acid and the danger of the work. To obviate this great trouble, Mr. Harrison, in 1814, introduced the use of platinum for the manufacture of sulphuric acid, for the first time, at least in this country. In the previous year, 1813, Dr. Eric Bollman, a Dane, had come to Philadelphia. Dr. Bollman was familiar with the metallurgy of platinum, and a highly scientific man. He brought with him from France Dr. Wollaston's method for converting the crude grains of platinum into bars and sheets. About the first use that Dr. Bollman made of these platinum sheets was the construction early in 1814, of a still for the concentration of sulphuric acid for the Harrison works. It weighed 700 oz., had a capacity of 25 gal. and was in continuous use for fifteen years. This early application of platinum for such purposes was highly characteristic of the sagacity and ingenuity of the American manufacturer. At the time the use of this rare metal was a novelty in Europe and known only to a few persons and certainly entirely unknown in this country. It follows, therefore, that Mr. John Harrison was not only the earliest successful manufacturer of sulphuric acid in America, but the first in this country to concentrate it in platinum."

Farr and Kunzi were next in Philadelphia to follow the lead of Harrison in making sulphuric acid, which it is stated they did in

1812, and shortly thereafter Wetherill & Bros. also began the manufacture of sulphuric acid on the east bank of the Schuylkill River. Chas. Lennig, the founder of the present firm of Chas. Lennig & Co., Inc., also began the manufacture of sulphuric acid in 1829, Rosengarten & Sons shortly thereafter, and Carter & Scattergood in 1834, also were early manufacturers of sulphuric acid.

Nitric acid, under the name of *aqua fortis*, is mentioned in Scharf & Westcott's "History of Philadelphia" as made by Christopher Marshall, Jr., a Philadelphia druggist, at the close of the last century. A communication from Mr. Thos. Skelton Harrison says his grandfather, John Harrison, began to make both nitric and muriatic acids in 1804. Carter & Scattergood had it on their list of manufactures in 1834. Muriatic acid is also mentioned as made by this latter firm in the year 1834, as were tartaric acid and citric acid.

#### MANUFACTURE OF PAINT COLORS.

The first white lead factory of Samuel Wetherill & Sons was built in 1804 at the corner of Broad and Chestnut Streets, but it was burned down a few years later, and in 1808, they erected a new factory at Twelfth and Cherry Streets.

"His son, Samuel Wetherill, Jr., was the active man of the concern, and assisted his father in all business matters. The enforced experience which was pressed upon them during the revolution, concentrated their attention upon the manufacture and sale of chemicals, and they went into the drug business. In 1785, Samuel Wetherill & Son were located in Front Street, above Arch. Here, for many years, 'Wetherill's Drug Store' was an old landmark, and the place at which sons and grandsons were brought up to the business. The Wetherills were the pioneers in the manufacture of white lead. They established it before the year 1790. They erected extensive white lead works near Twelfth and Cherry Streets, which were burnt down in 1813, but afterwards rebuilt.

"The fire which destroyed the white lead works proved to be incendiary and started by a young English officer the day before he sailed for England.

"In October, 1811, Samuel Wetherill, Jr., obtained patents for a new mode of washing white lead and for screening and separating metallic from corroded lead in the process of making red lead, and using the first machine ever used for manufacturing purposes



in the United States. This method has been generally adopted and used by all makers of lead.

"The name of the first white lead firm was Samuel Wetherill & Son, Samuel Wetherill, Jr., evidently being the active member. After his father's death in 1816, Samuel Wetherill, Jr.'s, sons joined the business and the firm became Samuel Wetherill & Sons. After the death of Samuel Wetherill, Jr., in 1829, it became Wetherill Brothers. The store of the firm was at 65 North Front Street; the warehouse and mill of the old establishment were on Coomb's Alley, back of Second Street.

"When the residence part of the city spread to Twelfth and Cherry Streets, Samuel Wetherill, having bought ten acres of land on the bank of the Schuylkill River, below Chestnut Street, moved there in 1847; his sons (Wetherill and Brother) built the white lead and chemical works and continue to this day."

John Harrison also began the manufacture of white lead in 1806. The firm of Mordecai & Samuel N. Lewis, which afterwards became John T. Lewis & Brothers, also began the manufacture of white lead in 1812, making three Philadelphia firms manufacturing paint colors at that time. These three earliest manufacturers of white lead and paint colors or their lineal successors have continued in business to the present time, for considerably over a century, and have done much to give Philadelphia its long-continued prominence as a chemical manufacturing center.

One of the lines of manufacture that contributed to make Philadelphia a great chemical center early in the last century was that of the yellow and red prussiates of potash. I have been furnished a private memorandum concerning the activities of the firm who began this industry and were active in it for many years.

"Under the firm name of Carter & Scattergood, a profitable chemical manufacturing business was conducted from 1834 to 1911; and was absorbed in the latter year by The Henry Bower Chemical Mfg. Co.

"John Carter and Joseph Scattergood bought out the old-established business of 'John & Daniel Elliott' founded in 1754 by their grandfather, John Elliott.

"Jos. Scattergood graduated P. C. P., 1829.

"The Elliotts' place of business and factory was originally on Front Street, between Chestnut and Walnut Streets, but in 1812, the manufacturing work was transferred to a new factory which

they erected at Nineteenth and Pine Streets, John Carter becoming their apprentice January 1, 1816.

"The list of chemicals produced by Carter & Scattergood was an extensive one, John Carter being the manufacturer and Joseph Scattergood, the business man of the concern. It included citric, tartaric, oxalic, nitric and sulphuric acids, bichromate and prussiates of potash and many other articles, but their operations during the first ten years of their business were on a scale which in this day would be considered quite small.

"Yellow prussiate of potash was first made by them in 1834 (that being, so far as known, the first production of the article in America), but the demand was very small, only 472 lbs. being absorbed by the market in that year. In 1835, the sales increased to 6443 lbs., but it was not until 1843 that the demand became large, the sales amounting in that year to 69,470 lbs. and rapidly increasing in the next two years, the sales in 1845 being 207,522 lbs.

"The high price, over 50 cents per lb., and the keen demand, of course, resulted in active competition, and the market for many years was over-supplied.

"In the year 1846, Carter & Scattergood began to produce red prussiate of potash, being the first in America. This was a highly profitable branch of the business until the introduction of coal-tar dyes, as substitutes for prussiate colors on woollen goods, gradually displaced it in the most important field of consumption. Except for the manufacture of *Blue-Print Paper*, there is now very little demand for it."

Potash and ammonia alums were first made in Philadelphia by Chas. Lenning in 1837 and by Harrison Bros. in 1840.

Coming now to the early manufacture of medicinal or pharmaceutical chemicals which has long made Philadelphia famous, we find that George D. Rosengarten and Charles Zeitler, as Rosengarten & Zeitler, began the manufacture of chemicals in St. John Street, Philadelphia, about 1822. They were the first to manufacture the alkaloids of cinchona and opium in this country, having begun the manufacture of sulphate of quinine in 1823, of sulphate of morphine in 1832, and strychnine in 1834. The salts of quinine were also manufactured by John Farr in 1825.

These two firms and their successors have had much to do with the establishment of Philadelphia as a chemical manufacturing center. After the withdrawal of Mr. Zeitler, which took place

within a year, Mr. Rosengarten continued alone, later taking in a Mr. Dennis. When this partner withdrew some twenty years later, the firm became Rosengarten & Sons, which business continued until the formation of the present combination with the other large Philadelphia manufacturer of medicinal chemicals, Powers & Weightman.

Farr & Kunzi began the manufacture of chemicals about 1818. Abraham Kunzi, a Swiss by birth, retired in 1838, and the senior partner, John Farr, who had been born and brought up in England, associated with himself Thomas H. Powers and William Weightman, two young Philadelphians who had been in the employ of the firm for some time. The new firm name was John Farr & Co. This was later changed to Farr, Powers & Weightman, and on the death of the senior partner in 1841, the firm name was again changed; this time to the title—Powers & Weightman, by which it was so long known throughout the entire country.

These two firms, in 1905, united under the name of the Powers-Weightman-Rosengarten Co., and continue as probably the best-known manufacturers of general and medicinal chemicals in the United States.

The history of the commercial production of pure glycerin is also of interest in this account of Philadelphia's chemical achievements.

The late Robert Shoemaker, while making medicinal plaster, had his attention directed by Professor Wm. Procter to the residuum liquid which was obtained. From this he prepared the first glycerin made in this city, if not in America, in 1846, and this was exhibited by Professor Procter to his class at the Philadelphia College of Pharmacy at that time. Mr. Shoemaker manufactured it for sale, according to his statement, for some years in connection with the manufacture of lead plaster.

The later development of the refining of waste lyes containing glycerin was also a Philadelphia achievement and was worked out by the late Henry Bower. By the courtesy of his son, Mr. W. H. Bower, I am allowed to quote from a private letter, which gives the account of his work, in his own words:

"Quite early in life, say in 1857, my attention was keenly directed to some mode of purifying these waste liquors of the stearine candle factories, and in that year I could have purchased the entire product of crude glycerine

of the United States for a sum not exceeding \$5000, although the manufacture of it was nearly if not quite as large then, as now.

"I commenced work in earnest to experiment in purifying glycerine in 1858—and expended long and weary efforts, all my earnings, as well as some borrowed money. I at first succeeded in producing an article sufficiently pure for use in gas meters (in place of alcohol) to prevent freezing and stoppage of the instrument—it was not however until about the middle of 1860 that I succeeded in making and placing in the market a 'pure inodorous glycerine,' even then the amount sold was quite insignificant. Inferior grades made their appearance about the same time in the West. The bland and neutral nature of the article, and the discovery of various uses for it, soon increased the demand to a marked extent; I was enabled from time to time to increase my works, and in increasing them was making steady inroad into the supply of the crude article. At this period, say in 1863, the business of refining glycerine was scarcely known on the continent of Europe, and I exported small quantities to Hamburg paying a profit; Belgium, France, Germany and Austria were immense producers of crude glycerine, but like its sister product here in previous years, it only found its way to the sea. As before stated, the use and sale of the refined continued to improve, the crude growing more scarce each season, until a point has been reached when every available pound is worked into a valuable product. It would not be out of the way to place the total value of all the glycerine sold in the United States at this time at \$500,000. This sum could never have been reached had it not been for the discovery of a mode for refining, to which, so far as this country is concerned, I lay claim; by a careful management of my business for some years I kept the process a secret; but in time some portions of it came to the knowledge of other persons, who have been enabled to produce very fair articles. There are besides myself, here, two refiners in Cincinnati, one in Chicago, and one in New York."

There were, of course, other drug and chemical firms who were well and favorably known in the early half as well as the later half of the nineteenth century.

We have already mentioned the name of Christopher Marshall, Jr., who was active in Revolutionary days. Himself the son of a druggist, he was succeeded by his son, Charles Marshall, and his grandson, Charles Marshall, Jr., who in 1814, established himself in the wholesale business at 310 Market Street.

With this Charles Marshall, Jr., entered as an apprentice, Geo. W. Carpenter, who later became one of the most prominent as well as successful of wholesale druggists in Philadelphia. The old store of Carpenter & Henszey at Eighth and Market Streets, I remember quite well as it stood about forty years ago.

A very well-known drug firm of the latter half of the nineteenth century was that of Bullock & Crenshaw. They were the

successors to Smith & Hodgson, who established themselves as druggists at the corner of Sixth and Arch Streets in 1819, where they continued until 1849, when they disposed of their drug business to two of their employees, who then formed the firm of Bullock & Crenshaw. This firm carried on not only a wholesale drug business but handled fine chemicals and chemical apparatus, supplying many colleges and schools throughout the country. In September, 1868, they moved to 528 Arch Street, where in larger quarters they carried on a flourishing business until the death of Mr. Chas. Bullock, the surviving partner.

The firm of French, Richards & Co. was for many years one of the best known of Philadelphia drug firms at its centrally located store, Tenth and Market Streets. The founder of this firm was Clayton French, who, in 1840, entered the drug business as an apprentice with Dr. Edward S. Wilcox. This firm was disbanded in 1890 on the death of its founder, but in the meantime its extensive cement and plaster department, which was started in 1852 at Callowhill Street and York Avenue, had been erected in 1883, into a separate business under the name of Samuel H. French & Co. This has since developed into a very extensive cement, plaster and dry color firm, now under the leadership of Howard B. French, a son of Samuel H. French of the original French, Richards & Co. firm.

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## URETHANES OF THYMOL AND CARVACROL.

BY D. C. L. SHERK.

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### METALLIC DERIVATIVES OF NITROSOPHENOLS.

By Brandel's<sup>18</sup> modification of the method of preparing nitroso-carcacrol and nitrosothymol, it is possible to obtain these derivatives in 95 and 96 per cent. of the theoretical yield, respectively.

The only derivative previously characterized definitely was the silver compound of nitrosothymol. Schiff<sup>19</sup> also obtained the "alkaliphenolates" in the form of long dark yellow needles when a solution of nitrosothymol in potassium or sodium hydroxide was allowed to evaporate slowly in a partial vacuum. Even the carbon dioxide of the air decomposed them. They were not characterized

<sup>18</sup> Kremers and Brandel, *Pharm. Rev.*, 22 (1904), p. 250.

<sup>19</sup> Schiff, *Ber.*, 8 (1875), p. 1500.

further. The derivatives of the heavy metals formed amorphous precipitates:

Pb = yellow  
Ca = yellowish-red  
Cu = bright green  
Zn = yellowish-white  
Cd = reddish-yellow  
Ag = deep red

Goldschmidt and Schmid<sup>20</sup> obtained the silver salt as a brown precipitate by adding silver nitrate to a solution of nitrosothymol in ammonia, and obtained, on analysis, 37.53 per cent. silver, compared with a theoretical content of 37.72.

For the preparation of alkali derivatives the corresponding nitrosophenol was dissolved in the theoretical quantity of 2N alkali, made up free from carbonate, and allowed to evaporate to dryness in a vacuum desiccator.

*Sodium Nitrosocarcvacrol.*—Nitrosocarcvacrol dissolves very readily in sodium hydroxide, giving a clear, reddish-brown solution, and evaporates, leaving a reddish-brown crystalline mass, with some bright green masses forming long thin crystals radiating in clusters. The crystals are ruby red by transmitted light, of rectangular shape, and pulverize to a maroon powder. This substance was stable at 100°. It decomposes suddenly and intumesces slightly on heating to a high temperature with evolution of reddish vapors and leaves a brown oily sublimate. It was dissolved in about six times its weights of absolute alcohol, filtered and precipitated by adding it to a large excess of ether. Reddish crystals appeared at once, and it was obtained as a bright maroon, crystalline powder. Sodium was determined by conversion into the sulphate and calculated to the basis of the substance dried at 100°.

0.3712 g. lost	0.0416 g. at 100°	
I. 0.2007 g. gave	0.0635 g. Na <sub>2</sub> SO <sub>4</sub>	
II. 0.2012 g. gave	0.0636 g. Na <sub>2</sub> SO <sub>4</sub>	
	Found	Calc. for C <sub>10</sub> H <sub>12</sub> NO <sub>2</sub> Na
Loss at 100°	11.21 p. c.	1H <sub>2</sub> O = 8.23 p. c.
		2H <sub>2</sub> O = 15.20 "
Sodium on dried basis	I. 11.30 p. c.	11.44 "
	II. 11.30 "	

The yield of sodium derivative recovered in this manner was 90.3 per cent. by weight.

<sup>20</sup> Goldschmidt and Schmid, Ber., 17 (1884), p. 2062.

*Sodium Nitrosothymol.*—Nitrosothymol dissolves in sodium hydroxide only slowly to a clear solution of a reddish-brown color. It forms a bright brownish-red mass of finely needle shaped crystals. It pulverized to a light brown (cocoa) colored powder. This was dissolved in absolute alcohol and poured into an excess of ether. The precipitate was amorphous, at first of rather an olive-green color. It quickly crystallized in brownish-red needles and on drying formed brown or bronze lumps with an orange fracture. It is stable at 100° and the sodium, determined as sulphate, is calculated for the dried product. It decomposes suddenly on heating, intumescenting splendidly, and spontaneously with sulphuric acid, giving a red sublimate.

	0.4407 g. lost	0.0622 g. at 100°	
I.	0.2004 g. gave	0.0618 g. Na <sub>2</sub> SO <sub>4</sub>	
II.	0.2013 g. gave	0.0617 g. Na <sub>2</sub> SO <sub>4</sub>	
		Found	Calc. for C <sub>10</sub> H <sub>12</sub> NO <sub>2</sub> Na
Loss at 100°		14.11 p. c.	1H <sub>2</sub> O = 8.23 p. c.
			2H <sub>2</sub> O = 15.20 "
Sodium on dried basis	I.	11.64 p. c.	11.44 p. c.
	II.	11.56 "	

The yield of sodium salt recovered in this manner was 95.7 per cent. by weight. It required much ether for its precipitation.

*Potassium Nitrosocarvacrol.* Nitrosocarvacrol dissolves very readily in potassium hydroxide, giving a clear reddish-brown solution. Evaporation of the solution left a crust of radiating clusters of very fine needles. The mass was blue-black in color, very finely granular and had not dried completely before taking up in absolute alcohol. This is less readily soluble than the sodium compound. It came out from ether as a tar, partially solidifying slowly to a blue-black mass like iodine. The solid is bright and pulverizes to a bright green powder. A tar remained which solidified on exposure. It was dried at 100° and the potassium estimated as sulphate. The mass swelled up slightly on heating and a red-brown sublimate formed.

	0.3207 g. lost	0.0231 g. at 100°	
I.	0.2000 g. gave	0.0762 g. K <sub>2</sub> SO <sub>4</sub>	
II.	0.2004 g. gave	0.0758 g. K <sub>2</sub> SO <sub>4</sub>	
		Found	Calc. for C <sub>10</sub> H <sub>12</sub> NO <sub>2</sub> K
Loss at 100°		7.20 p. c.	1H <sub>2</sub> O = 7.66 p. c.
Potassium on dried basis	I.	18.42 p. c.	18.00 "
	II.	18.30 "	

This was recovered from ether in only 81 per cent. yield by weight.

*Potassium Nitrosothymol*.—Nitrosothymol dissolves somewhat readily in potassium hydroxide, leaving an oil-like film on the surface. It evaporates leaving a bluish-green mass with a green fracture and not well crystalline. It forms an olive-green powder. When dissolved in absolute alcohol, it begins to come down on adding an equal volume of ether. It forms a bright mass of almost malachite green with a bright fracture. It is stable at  $100^{\circ}$ , but decomposes spontaneously with sulphuric acid, and on heating, giving a bright red sublimate.

0.4210 g. lost	0.0334 g. at $100^{\circ}$	
I. 0.2000 g. gave	0.0756 g. $K_2SO_4$	
II. 0.2040 g. gave	0.0772 g. $K_2SO_4$	
	Found	Calc. for $C_{10}H_{12}NO_2K$
Loss at $100^{\circ}$ ,	7.93 p. c.	
Potassium on dried basis	I. 18.42 p. c.	$1H_2O = 7.66$ p. c.
	II. 18.44 "	18.00 "

It was recovered in 91 per cent. yield by weight; ter Meer<sup>20a</sup> prepared the alkali compounds of nitrosophenol itself by allowing a solution of the metal in absolute alcohol to act on an ether solution of the nitrosophenol. He crystallized his products from water and acetone and found them stable towards carbon dioxide in aqueous solution. The ammonium compound was unstable and could not be prepared at all.

The sodium derivative of carvacrol forms the most readily, and is of the finest appearance. It is immediately crystalline by precipitation from ether and dries as a splendid, brown maroon powder. The thymol derivative comes out amorphous at first, but quickly becomes crystalline, and gives needles of much the same color, cementing to lumps on filtration and drying. The potassium compounds give aqueous solutions of much the same color, but blue solids from water and ether. They appear as amorphous oils and the thymol compound crystallizes most readily, contrasting with sodium in this. It comes out easily. Thus on precipitation by ether the order is this:

- Sodium derivative of carvacrol.
- Potassium derivative of thymol.
- Sodium derivative of thymol.
- Potassium derivative of carvacrol.

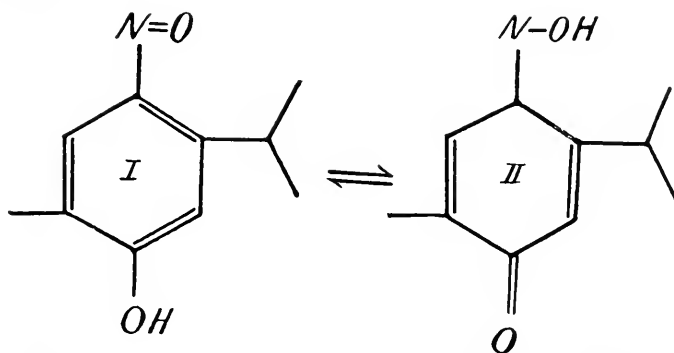
<sup>20a</sup> ter Meer, Ber., 8 (1875), p. 622.



This last derivative behaved very badly, yielding an exceedingly deep blue colored amorphous mass, which solidified very slowly.

The difference in color is very striking. ter Meer<sup>21</sup> obtained the potassium salt of nitrosophenol in a similar manner and found it to exhibit another form. It came out as a green amorphous precipitate from ether, which, if moist, passed easily into the red crystalline form. Form alcohol or acetone, it formed thin blue-green plates, sometimes in a red form, probably of a different water content. Beilstein<sup>22</sup> is inclined to doubt this supposition.

The loss at 100° for the potassium derivatives corresponds very closely to that required for one molecule of water of crystallization; while that for the sodium derivatives corresponds somewhat to that required for two molecules of water, as ter Meer found for the sodium derivatives of nitrosophenol itself. This difference does not extend to their aqueous alkaline solution because both the sodium and potassium derivatives give the same benzoyl compound. The difference may be one of isomerism as two forms of the phenol derivative are possible, or it may represent an equilibrium mixture with only a little of one form present with the other.



The first (I) is the true nitroso form, and the second (II) is the "isonitroso" or oxime type.

*Structure of Metallic Nitroso Derivatives.*—The true nitroso form of these phenols is supposed to exist, because the mixture containing nitrous acid in their preparation may be bright blue or greenish. On the other hand, the blue and red salts or alkali deriva-

<sup>21</sup> ter Meer, Ber., 8 (1875), p. 622.

<sup>22</sup> Beilstein, 3d ed., vol. II, p. 678.

tives have been considered derivatives of the oxime and nitroso types respectively and may be illustrated thus:

Inhaling the powder of these substances effects the mucous membrane of the nose and readily causes sneezing. They are decomposed by carbon dioxide in aqueous solution. The solutions of the nitroso derivatives in the hydrocarbons heptane and benzene were treated with sodium and heated for hours in the water bath, but the action was very slight. No perceptible evolution of hydrogen took place and with the thymol derivative the sodium retained its metallic luster for weeks in contact with the solution.

The silver derivative of nitrosocarvacrol was prepared by the action of silver nitrate solution on an equivalent of the oxime dissolved in the theoretical quantity of 2N potassium hydroxide. A greenish-brown mush formed, later turning to olive and finally brown. Brandel<sup>22a</sup> prepared this compound in a similar manner, but observed the reverse color changes from brown to green. The precipitate was granular and washed readily at the pump, after which it was dried in the air. It is a brown powder, stable in the air. It is slightly soluble in water and imparts a reddish color after boiling. During heating an odor is apparent and it melts together in the hot water. The yield was about 90 per cent. of the theoretical by weight. It was analyzed for silver by ignition, after drying in a vacuum desiccator. It melts on heating and gives a red-brown sublimate.

I. 0.4048 gm. gave 0.2485 gm. silver.

	Found	Theory for $C_{10}H_{12}NO_2Ag$
Silver	36.64 p.c.	37.72 p. c.

Brandel obtained values for silver of 36.66 and 36.84 per cent., but assigns the formula  $C_{10}H_{12}NOAg$  (no doubt unintentional), which requires 39.95 per cent. of silver. In addition he observed a considerable solubility of the silver salt in cold distilled water and separated a precipitate containing 54.36 and 54.1 per cent. of silver. He assigns to it the formula  $C_{10}H_{11}NOAg_2$ , whereas the silver content required for  $C_{10}H_{11}NOAg_2$  is 54.91 per cent. No such combination was observed, however, in this work.

The silver derivative of nitrosothymol has been prepared by Goldschmidt and Schmid.<sup>22b</sup> It was prepared in the same manner as

<sup>22a</sup>Kremers and Brandel, Pharm. Rev., 22 (1904), p. 250.

<sup>22b</sup>Goldschmidt and Schmid, Ber., 17 (1884), p. 2062.

the carvacrol derivative. The color of the precipitate appeared reddish at first, changing to brownish-black. It was filtered and washed with difficulty because it remained gelatinous. After drying in a vacuum desiccator, as with the other, it became grayish-brown and lost its luster. It is bulky and somewhat unstable in light as the exposed surfaces become gray on standing. It has a slight odor; melts under hot water, and the solution also has a slight odor; while its color is bright yellow, with no tinge of red, as with the carvacrol compound. It was obtained in 90 per cent. yield by weight. It was analyzed for silver by ignition. It did not melt, but gave a splendid purple sublimate.

	Found	Calculated
I. 0.4368 gm. gave 0.1707 gm. silver.		
Silver	39.08 p. c.	37.72 p. c.

The colored sublimates obtained on heating all of the metallic derivatives of nitrosophenols are to be considered azo-derivatives; since Beilstein<sup>22c</sup> attributes to Jaeger<sup>23</sup> the statement that nitrosophenol heated with potash to 180° gives azophenol,  $C_{10}H_{12}N_2O_2$ .

A small quantity of substance was heated gently in a test tube and the sublimate examined to ascertain its character. In every case it was crystalline, but the color varied somewhat and the crystalline form varies, there being at times two or more strikingly different forms of crystals.

The silver compound of carvacrol forms an oxblood or maroon sublimate, which appears as yellowish amorphous droplets that crystallize after a time. The thymol compound gives a bright reddish-purple sublimate, which crystallizes in stellate groups.

The sodium compounds form needles, pointed at both ends, of a very pale brownish or reddish-brown color. Thymol forms in addition rhombic crystals with characteristic surface markings. The potassium compounds give sharp needles appearing in clusters, but the sublimate is blue rather than brown.

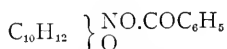
#### BENZOYL DERIVATIVES OF NITROSOPHENOLS.

Part of the interest in the preparation and study of these derivatives lay in the fact that they might throw light on the structure of the alkali derivatives.

<sup>22c</sup>Beilstein, 3d ed., vol. II, p. 678.

<sup>23</sup>Jaeger, Ber., 8 (1875), p. 895.

The thymol compound was first prepared by Schiff <sup>23a</sup> by the action of benzoyl chloride on the potassium salt. The mixture was melted together on the water bath, when it solidified. It was purified and crystallized from absolute alcohol or chloroform as beautiful yellow glistening needles with a melting point of 110° (uncor.). An analysis is given corresponding to the formula C<sub>17</sub>H<sub>17</sub>NO<sub>3</sub>. Godschmidt and Schmid <sup>23b</sup> prepared the same derivative by using the sodium compound. It melted at 110-111°. The nitrogen content is correct. The sodium and potassium compounds give the same derivative. These authors assign the ketone structure to this derivative.



These were prepared by the Schotten-Baumann reaction, using one-fortieth mol of reacting substances:

Nitrosophenol 4.5 gm.  
Benzoyl chloride 3.5 gm.  
Sodium hydroxide 1.0 gm.

The nitrosophenol was dissolved in the equivalent quantity of 10 per cent. sodium hydroxide solution and benzoyl chloride added with shaking till an odor persisted to ensure an excess.

*Nitrosothymol* dissolves in the sodium hydroxide with evolution of heat. The chloride was added from a pipette and the stoppered flask shaken. The reaction product separated out as orange colored granules, which were not melted by the heat of reaction. It was filtered at the pump and washed with water, and dried over night on paper. The product so obtained weighed 7.6 g. with a theoretical of 7.07 g. It melted at 105°, and after freezing at 97-105°.

This was crystallized from 95 per cent. ethyl alcohol, in which it is readily soluble and crystallizes well.

		M. P.
First crop,	5.47 gm.	109.5-110.5°
Second crop,	0.59 gm. diluted with water.	109.0-109.5°
Third crop,	0.23 gm. Brown tarry.	
Total,	6.29 gm.	
Yield,	89 per cent.	

10.8 gm. nitrosothymol dissolved in the equivalent quantity of 2N potassium hydroxide gave 13.93 gm. benzoyl derivative, a yield

<sup>23a</sup> Schiff, Ber., 8 (1875), p. 1500.

<sup>23b</sup> Godschmidt and Schmid, Ber. 17 (1884), p. 2062.

of 82 per cent. It was crystallized from 30 cc. 95 per cent. alcohol, but caused trouble by clogging a filter.

The thymol compound is bright yellow, with an orange tint which deepens on exposure—it is somewhat sensitive in this respect—and forms thick needles. It is readily soluble in heptane and crystallizes out as a mush of pale yellow crystals. The solution in alcohol is deep orange, almost brown, but somewhat lighter in heptane. The alcoholic solution develops an odor of ethyl benzoate, showing that alcoholysis takes place.

*Nitrosocarvacrol* dissolved in the sodium hydroxide with evolution of heat. The benzoyl chloride warmed the reaction mixture and an oil formed which solidified slowly and as a film of brownish-yellow color on the walls. It was washed at the pump and dried. It weighed 7.4 g. It melted between 74° and 85°. This was crystallized from 95 per cent. ethyl alcohol, in which it is more readily soluble than the thymol derivative and crystallizes well.

M. P.  
 87°  
 85°

First crop,	6.013 gm. diluted with water.
Second crop,	.93 gm.
Total,	6.94 gm.
Yield,	98 per cent.

10.8 gm. nitrosocarvacrol dissolved in the equivalent quantity of 2-N potassium hydroxide, gave 16.39 g. benzoyl derivative with a yield of 96 per cent.

This compound forms rectangular plates with bevelled edges of bright yellow color with orange tint, stable in the air. It is more soluble than the thymol compound. The alcoholic solution is deep orange to brown and develops an odor of ethyl benzoate. The solution in heptane is brownish in color and deposits on cooling or evaporation, yellow prisms.

The characteristics of the sodium and potassium derivatives of nitrosophenols are apparently not different in this reaction, because 10 per cent. sodium hydroxide gave yields that are almost quantitative and the same for 2-N potassium hydroxide.

Alkali	Carvacrol	Thymol
NaOH (2-N) 11 p. c.	96 p. c.	89 p. c.
KOH (2-N) 11 p. c.	96 "	82 "

The brilliant color of these products resembles that of thymoquinone so strikingly that the ketone structure was suggested for them

These compounds should prove more useful for purposes of identification of these two phenols than the nitroso compounds themselves. These may be derived from the nitroso compounds in one step. They are easily purified, slightly sensitive to light and air only when moist, and are stable at the melting point. The difference in melting points is  $22^{\circ}$  compared with the difference of  $9^{\circ}$  between the nitroso compounds which are unstable at that point, and nitrosothymol scarcely has a melting point, unless it has been very carefully purified. It is impossible to separate these compounds, and thus thymol and carvacrol in the presence of each other cannot be distinguished. With more stable compounds like the benzoyl or similar derivatives a separation may become possible. The crystalline forms of the benzoyl derivatives are strikingly different also.

#### OXIMES OF BENZOYL DERIVATIVES.

In view of the fact that the ketone structure has been assigned arbitrarily to these derivatives, which the similarity in color with thymoquinone supports, an attempt was made to prepare an oxime. The molecular quantities, in one hundredth mol, were used. First the alcoholic solution of the benzoyl derivative was treated with hydroxylamine hydrochloride and potassium hydroxide.

Benzoyl derivative,	2.83 gm. in 20 cc. alcohol.
Hydroxylamine hydrochloride,	0.7 gm. in 20 cc. water.
Potassium hydroxide,	0.7 gm.

5 cc. 2N Potassium hydroxide were used and the mixture was heated under a reflux condenser in a water bath for three hours. The orange solution in alcohol turned brown on addition of the alkali and enough was added to give just such a permanent brown color. The reaction mixture was poured into water to dissolve the salt and precipitate the alcoholic solution. The carvacrol derivative first gave an oil which later solidified to a flocculent precipitate. The thymol compound gave a heavy, flesh-colored precipitate at once. The liquid smelled strongly of ethyl benzoate. The precipitates were filtered, washed and dried, and weighed and the melting point determined.

	Weight	M. P.
Carvacrol,	1.54 gm.	142° with decomp.
Thymol,	1.62 gm.	158.5° with decomp.

They were soluble in alkalis and ammonia with a brown color and conducted themselves like the original nitrosophenols. Recrystallized from heptane they melted as follows:

	M. P.	M. P. of nitrosophenols
Carvacrol,	151°	153°
Thymol,	161-162°	160-162°

If conversion into the nitroso derivative be complete, the yield should be 1.79; accordingly that gives:

Carvacrol,	86.0 p. c.
Thymol,	90.5 "

It, therefore, becomes apparent that in the presence of alkali the benzoyl group is split off, regenerating the original nitroso-compound:

The brownish-red color obtained on adding an excess of alkali is apparently that of the nitrosoalkali derivative. Heating in the water bath for three hours is sufficient to complete this hydrolysis. An insufficient amount of alkali might delay this reaction. The filtrates had the odor of ethyl benzoate, strongly, but gave no precipitate on addition of sulphuric acid, and no attempt was made to isolate benzoic acid. The pale yellow color of the liquors showed just a perceptible darkening with sodium hydroxide, which may be attributed to the nitroso compound remaining in solution.

Next the reaction was carried out in heptane solution, using sodium bicarbonate to liberate hydroxylamine. Equivalent quantities were taken:

Benzoyl derivative,	0.71 gm.
Hydroxylamine hydrochloride,	0.18 gm.
Sodium bicarbonate,	0.21 gm.

These substances were finely pulverized and mixed and 10 cc. heptane added as a reaction medium.

Over night the appearance of both mixtures had changed. The carvacrol reaction mixture contained fine needles reaching to the surface of the heptane. On heating in a water bath the entire mixture became crystalline and granular with a rim of crystals adhering

to the flask. The thymol reaction mixture formed a mush of crystals that fluffed up and filled the liquid completely. Both mixtures were extracted repeatedly with heptane and allowed to crystallize after each extraction. The carvacrol mixture gave finely granular yellow crystals; while the thymol mixture gave a gelatinous precipitate which filtered with difficulty and dried to a pale yellow film.

		M. P.
Carvacrol,	1st crop	129°
	3rd crop	134-135° no evolution of gas.
Thymol,		146-147° with decomp.

The heptane solution of carvacrol gave a few crystals on evaporation which gradually acquired a bright red color and a peppery odor. That of the thymol evaporated leaving a pale cream colored amorphous film which did not become discolored. It had a very faint peppery odor. The amount of each recovered by crystallization from heptane represented a yield of 68 per cent. for carvacrol and 62 per cent. for thymol.

These substances dissolve in alcohol with a reddish to yellowish color and on addition of water become turbid, and finally deposit crystals. Those for carvacrol are very long hairlike, those for thymol short glistening prisms. The quantity was too small to work with, but melting points were determined.

		Carvacrol	Thymol
1st sample,	Soft	164°	163-165° decomp.
2nd sample,	152°	165-166°	165-166°
Oxime in parallel,	128°	132°	146-149°

These may be the original nitroso compounds, but they appear to be the same substance.

Alkalis give an immediate red-brown color, showing decomposition, but a precipitate remains even after boiling. The possibility of formation of the dioxime above is considered, but this should be soluble in alkali, and melts after crystallization from alcohol, at 255° with decomposition. This apparently rules out the product melting at 165°. It may be that hydrolysis takes place in such a manner that each gives the same isomeric form, namely, nitrosothymol.

Further quantities of the oximes were prepared, using 5.56 g. benzoyl derivative in 50 cc. heptane. Carbon dioxide was given off very soon, and on standing in the cold pressure developed continu-



ously in the flasks. They were heated for three-fourths of an hour in the water bath. The carvacrol reaction mixture became reddish-brown in color and a granular deposit formed. The thymol mixture formed a mush of crystals that contained both yellow and brown particles. These mixtures were extracted with heptane and the residues washed with ether and tested for hydroxylamine and carbonates. That from the carvacrol mixture gave a wholly negative test with Fehling's solution, but the reaction for carbonates was positive. That from thymol gave positive reactions for both, showing that the reaction was not so nearly complete as in the case of carvacrol.

The ether and heptane extracts were crystallized from benzene, in which the carvacrol compound is very readily soluble and forms spherical aggregates of fine needles. The thymol compound is less readily soluble and forms a thick mush that was somewhat gelatinous. Both are pale yellowish powders stable in the air.

#### *Carvacrol Compound.*

From benzene sinters at 110°, melts at 133-136°, turning brown.

From heptane sinters at 110°, melts at 137°, turning brown.

#### *Thymol Compound.*

From benzene sinters at 145°, melts at 156-157°, with evolution of gas.

Recrystallized from chloroform sinters at 158°, melts at 158-159°, with decomposition.

These two substances were analyzed for nitrogen by Dumas' method:

Carvacrol derivative 0.3000 gm. gave 30.0 cc. N<sub>2</sub> at 25° and 708 mm.

Thymol derivative, 0.2556 gm. gave 17.9 cc. N<sub>2</sub> at 26° and 707 mm.

Nitrogen Found		Calculated for	Calculated for
		C <sub>17</sub> H <sub>18</sub> N <sub>2</sub> O <sub>3</sub>	C <sub>10</sub> H <sub>13</sub> NO <sub>2</sub>
		benzoyl-oxime	nitroso derivative
Carvacrol,	10.7 p. c.	9.40 p. c.	—
Thymol,	7.5 "	—	7.82 p. c.

It is thus apparent that the benzoyl derivative of carvacrol reacts to form the oxime; while that of thymol does not form the oxime, but is hydrolyzed, regenerating the original nitrosothymol under the same conditions. This accounts for the hydroxylamine remaining in the residual salts of the thymol reaction mixture. Since, therefore, the nitroso compound exists, the red-brown color with the alkalis is due entirely to this; and carvacrol, because it

behaves similarly, must be broken down to the nitrosoderivative by alkali. It is very interesting to note that apparently nitrosothymol and not nitrosocarvacrol results by this decomposition.

#### THE ALKYL ETHERS OF THE NITROSOPHENOLS.

The formation of alkyl ethers from the different metallic nitrosoderivatives was undertaken in an attempt to differentiate between the two possible types. Since the nitrosophenols may exist in two forms ethers should exist in two forms also by replacement of the hydrogen by an alkyl radical.

Bridge<sup>24</sup> obtained a methyl ether of nitrosophenol itself in two manners. The silver derivative of nitrosophenol and methyl iodide were allowed to react in dry ether. By the action of the sodium derivative in methyl alcohol on methyl iodide the same compound was obtained. The yield was rather low and much polymerized nitrosophenol resulted.

That the methyl group was in the oxime and not in the phenol group was proven in the case of another derivative, the benzoyl ether, which was obtained quantitatively from quinone and  $\alpha$ -benzylhydroxylamine:

Goldschmidt and Schmid<sup>24a</sup> found that the action of methyl iodide on the silver derivative of nitrosothymol gave only tars from which the original nitroso compound could be regenerated. An attempt was made to prepare the methyl derivatives of both phenols in a similar manner. Four grams of the silver derivative were mixed with the theoretical quantity of methyl iodide and the mixture warmed with a little alcohol under a reflux condenser. There resulted a brown solution and a very pale residue. The carvacrol reaction mixture was filtered and the residue digested with dilute nitric acid. Chlorides gave a copious precipitate, showing that much of the silver compound remained undecomposed. Boiling with concentrated nitric acid left practically no residue, showing that little silver iodide had been formed during the reaction. The thymol reaction mixture was steam distilled, but practically nothing was separated in this manner.

<sup>24</sup> Bridge, A. C. J., 14, p. 276.

<sup>24a</sup> Goldschmidt and Schmid, Ber., 17 (1884), p. 2062.

The reaction was next carried out with the alkali derivatives in alcoholic solution; 4.5 g. nitrosophenol were treated with 1.5 g. potassium hydroxide in 15 cc. methyl alcohol previously distilled over potassium hydroxide. To this were added 3.6 g. methyl iodide and the mixture tightly stoppered and shaken frequently. By morning crystals had deposited and the reddish-brown color of the solution remained but the odor of methyl iodide had disappeared. The crystals were easily proven to be potassium iodide, and the alkaline reaction had disappeared from the solution. The reaction mixture was allowed to evaporate spontaneously and the white crystals washed free from adhering liquor with ether. Both of the phenols gave brown oils at this point. Carvacrol gave a yield of potassium iodide of 87 per cent.; while that for thymol was lost. The brownish-black ethereal solution was shaken with dilute hydrochloric acid to remove basic constituents. This was made alkaline and again shaken with ether. Both ether solutions were evaporated spontaneously. Nothing appeared from the acid wash liquors.

The oil obtained from carvacrol solidified. The compound is probably the oxime ether. The crystals were pressed between paper and melted at  $39^{\circ}$  and were stable up to  $144^{\circ}$ . They are bright yellow or orange crystals of needle shape. The oil from thymol remained liquid. It was accordingly steam distilled. It formed a yellow layer in the distillate lighter than water and came over about as fast as the methyl ether of carvacrol, and accordingly cannot be considered readily volatile as the acetone derivatives have been described.<sup>25</sup> The later distillate came over red and was heavier than water. The aqueous portion was extracted with ether and dried over calcium chloride with no apparent change in the chloride. The separated oil was also dried over calcium chloride when the lumps of chloride began to disintegrate and formed a fine powder somewhat in the manner that calcium chloride forms alcoholates. When the oil itself was diluted with ether and allowed to stand over the chloride, the same change was noticed after ten days.

The analysis of the crystalline methyl derivative of carvacrol gave the following results by Dumas' method:

0.2222 g. gave 15.3 cc.  $N_2$  at  $25^{\circ}$  and 708 mm.

	Found	Calculated for $C_{11}H_{13}NO_2$
Nitrogen,	7.40 p. c.	7.26 p. c.

<sup>25</sup> Diels and Plaut, Ber., 38 (1905), p. 1917.

The potassium derivatives of the nitrosophenols were shaken with methyl iodide in heptane solution. The odor of the iodide persisted for several days and no perceptible change took place in the alkali derivative. The thymol finally changed to a pale, fluffy powder, but the carvacrol remained as a heavy dark precipitate.

After several weeks in contact with the heptane solution of methyl iodide, the heptane gradually acquired a reddish color and the residue changed, losing its dark, almost black color and forming an adherent precipitate. Apparently the reaction was taking place with formation of colorless potassium iodide.

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### THOMAS FRANZ HANAUSEK.

By A. L. WINTON,

WILTON, CONN.

Dr. Hanausek died at Vienna, on February 4, 1918, in the sixty-sixth year of his age. He was elevated by the Emperor to the rank of Hofrat for gratuitous service in the examination of foods during the war, but the decoration did not arrive until two days after his death. Necrologies appeared in the leading Austrian and German scientific journals, but few if any of these reached America, and his death was not learned by even his close friends at a distance until long after. I was in correspondence with him during 1914 and 1915, but letters became more and more delayed and finally were not transmitted at all. His letters were filled with sad tales of the suffering caused by the war, but were noteworthy for the absence of rancor. He wrote that his only son, a young lawyer in Vienna, had been called to the colors, although he had never served as a soldier because of his weak lungs. "The poor devil," so wrote his father, "must carry 50 kilograms of baggage, a heavy gun, and, what was hardest of all with his short breath, run."

Just before the United States entered the war this same son wrote me from a Russian prison camp, begging that I inform his father, who had not heard from him since he was taken prisoner, that he was alive and slowly recovering from a severe wound. He also asked for literature in the French language to relieve the tedium of his confinement. To both requests I complied, sending



THOMAS FRANZ HANAUSEK.



messages and parcels through official channels, but neither reached their destination. So also the death of his father was unknown to the son until he was released and returned to Vienna.

Rather than detail the events in Hanausek's busy life and compile a long list of his publications, I will attempt to give an insight into his keen scientific acumen and inspiring character by a few reminiscences.

While carrying on some work in Moeller's laboratory at Graz in 1904, I was filled with a desire to meet Hanausek, whom I had come to know through his publications. I accordingly wrote him at Krems-on-the-Danube, begging an interview. When I reached my hotel at Vienna, I found a black bordered letter, not only granting my request but giving full directions as to trains. Arriving at Krems, not knowing he was at the station, I took a conveyance to his house, where he soon joined me. With an awkward click of the heels and stiff bow I apologized for taking his time, but stated that having read and reread his books I was eager to meet the author himself. He at once put me at ease, saying that he had unlimited time when a friend came 4000 miles to see him.

He then inquired which of his books I had. I said *Lehrbuch der technischen Mikroskopie* and *Die Nahrungs- und Genussmittel aus dem Pflanzenreiche*. He turned to his book shelves and took down copies of his *Lehrbuch der Somatologie und Hygiene* and his revision of *Weidinger's Waarenlexikon der chemischen Industrie und der Pharmacie*, wrote my name on the flyleaves, and handed them to me in commemoration of the visit. When I then hinted that I would make my call short, he said I could not get back to Vienna until night and that I was his guest until then. He added, with a sigh, that since his wife's death he lived alone, except for his servants, and he would be glad if I would spend a week or two with him. All of this cordiality to an obscure stranger overwhelmed me.

On my part it was love at first sight and I at once found him the most magnetic man I had ever met. That day lingers in my memory as perhaps the most delightful of my life. A ride into the beautiful Wachau to Dürnstein, where he showed me the castle in which Richard the Lion-Hearted was imprisoned and before which Blondel sang his song—so tradition would have it, although, as Hanausek explained, this was a beautiful myth. Then a visit to the

gymnasium, of which he was director, a dinner such as one eats only in an Austrian home, a discussion of work and workers, postal cards to the latter and, as mementoes, even to ourselves—a wonderful day with a wonderful man.

My translation of his *Lehrbuch der technischen Mikroskopie* was a consequence of this visit.

While in Vienna for a week during the summer of 1914, my wife and I saw him every day. We talked of our work and that of Vogl, Moeller, Tschirch, Von Höhnelt, Wiesner, Hartwich and others. We dined at his house, where we enjoyed Frau Hanausek's viands and rendition of Wagner, for she was formerly the prima donna at the Hanover Opera. His beautiful daughter, to whom he once referred as the sunshine of his lonesome life, having gone on the stage, was seldom with him, and his second marriage was a great consolation. Vienna is quite as much the home of applied vegetable histology as it is of music, and it has been my privilege to have drunk of both at the fountain head.

During a visit to the Burg, Hanausek pointed out the windows lighting the corridor, where as a young officer he paced in front of the Empress Elizabeth's apartments during the night watches. At Schönbrunn he showed me where the Emperor Franz Josef then lived and gave me bits of his history learned at close range. Once—a Roman Catholic himself—he spoke dramatically of the influence of the Jesuits on the Crown Prince Rudolf and the resentment of certain classes. I asked if the Emperor himself was not also under the same influence, to which he replied, "Yes, but he is beloved by the people." We little thought that already the plot for the assassination of the Crown Prince had ripened and in a week would be consummated.

After the armistice, when mail routes to Austria were again opened, I sent Hanausek a card to the effect that we were again officially friends, adding that we had never been personally anything else. In due time acknowledgment came from his widow in a touching letter, stating that he died two years before. She said his study was just as he had left it, with books, apparatus, photographs of his friends in place, as it seemed to her that he must come back again. To his friends this sentiment is understandable as his influence so lives with us as to make his death seem unreal.

As a scientist Hanausek was versatile, but never mediocre. He



was alike at home in pure and applied science. His papers on the humus layer of the *Compositae* published in the *Denkschriften der mathematisch-naturwissenschaftlichen Klasse der kaiserlichen Akademie Wissenschaften* and the *Berichte der deutschen botanischen Gesellschaft* are classics which will survive as long as the study of vegetable histology. In the applied field he has no peer, whatever the branch—drugs, foods, textiles, paper, wood or even horn and bone. The practical examples given in his *Lehrbuch der technischen Mikroskopie* illustrate his remarkable genius in unravelling court mysteries by the aid of the microscope. They read stranger than any detective fiction.

Of my several photographs of Hanausek, I prize most one bearing his signature and the motto to which he owed his success—*“Das Beste im Leben ist die Arbeit”* (The best thing in life is work). He was never idle, and he died in the midst of a busy life.

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## ABSTRACTED AND REPRINTED ARTICLES

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### AN EXPERIMENTAL STUDY OF ECHINACEA THERAPY.\*

BY JAMES F. COUCH AND T. GILTNER. (Pathological Division,  
Bureau of Animal Industry, U. S. Dept. of Agriculture.)

This investigation was undertaken for the purpose of determining the usefulness of echinacea as a remedy in several pathological conditions induced by bacteria, their products, or allied toxins. The experimental animals used were guinea pigs. The preparations of echinacea employed as remedies were the “Specific Medicine Echinacea” and the “Subculoyd Inula and Echinacea” both prepared and furnished by Lloyd Brothers of Cincinnati, and the Fluidextract Echinacea, N. F. 4. The acute experimental pathologi-

\* Author's Abstract of article in *Journal Agric. Research*, vol. 20; No. 1, pp. 63-847, 1920.

cal conditions produced in the guinea pigs were tetanus and botulism (in both of which the diseases were produced by bacterial toxins), anthrax and septicæmia (in both of which the bacteria were injected into the animals), and crotalus poisoning (in which the venom of the rattlesnake was injected). The chronic diseases against which the echinacea preparations were tested consisted of tuberculosis and a trypanosomiasis (dourine), the first of which was produced by inoculation with the bacillus from a human strain, and the second by inoculation with the trypanosomes. The pathogenic materials were carefully selected and were tested for activity and potency so that no animal should receive an excessive dose.

The method of procedure was designed to favor the remedy as much as possible. Both *per se* and parenteral administration of the remedy was employed. Some of the animals were injected with the pathogenic material and were immediately afterwards treated with the echinacea preparations in suitable doses the treatment being continued until the animals succumbed. Other animals were dosed with echinacea for several days before administering the organism or toxins and then were given remedial doses. Still others were given a few doses of echinacea and were then rested for several days and were finally injected with pathogenic material.

In no one of the diseases treated with echinacea preparations was any evidence obtained to show that the plant exerts any influence upon the course of infectious processes under laboratory conditions. In the two chronic diseases where the animals were given doses of echinacea for extended periods of time nothing appeared in the autopsy pictures which could be attributed to the action of the echinacea *per se*, except that in two cases a gastric catarrh was present which may have been due to this plant. Every experiment was checked with control animals in sufficient number and, in all cases, the course of the disease was the same in the control animals and in the animals which were given remedial treatment.

It does not appear, therefore, that the preparations of echinacea are of value in the treatment of diseases produced by micro-organisms and their toxic products.

COMMENT ON THE PAPER BY COUCH AND GILTNER  
ON "AN EXPERIMENTAL STUDY OF ECHINACEA  
THERAPY."

By JAMES H. BEAL.

It is regrettable that a larger proportion of the interesting paper by Couch and Giltner is not covered by the abstract, especially the tables of experiments, since it is from a study of the latter that we are able to appreciate the difference in the methods of deduction commonly employed by the laboratory worker than those employed by the clinician who administers a drug with therapeutic intent.

In these experiments various authentic preparations of echinacea, or of echinacea combined with inula, were administered to guinea-pigs either prior to or subsequent to intoxication or infection with various poisons or organisms, and the results compared with those observed in control animals with the same intoxications or infections, but which did not receive echinacea treatment.

In the experiments with tetanus 25 animals were each given 3 times the minimum fatal dose of a carefully standardized tetanus toxin. Six of the animals were kept as controls, while the remainder received treatment with echinacea. All of the poisoned animals died, but whereas the average survival period of the controls was approximately 2.25 days, the average survival period of the echinacea treated animals (so far as it can be determined from an inspection of the table) was approximately 2.65 days.\*

The authors' conclusion is that "neither the protective treatment nor the remedial treatment, nor a combination of the two appeared to influence the course of the disease," but the average clinician would be inclined to maintain that the results as stated in the table show a perceptible margin of evidence in favor of echinacea treatment.

In the experiments with botulinus toxin, ten times the minimum fatal dose was administered to each of five guinea-pigs, of which two were kept as controls. As shown by the table, the average

\*In these calculations the statement "less than 3 days" is taken as 2½ days for both controls and treated animals. Twenty-nine animals were used, but four of them were employed in a side test with alcohol of the same strength as the echinacea preparations.

survival period of the controls after receiving the toxin was 2 days, while the average survival period of the echinacea treated animals was 2.33 days.

The authors' conclusion is that "it does not appear that echinacea possesses remedial value against botulism," while a clinician might urge that the figures in the table actually show perceptible remedial value for the drug in such cases.

In the septicemia experiments 13 animals were subjected to doses of a pathogenic culture of *Bacillus bovisepcticus*. Three of the animals were reserved as controls, of which two died and one recovered, the average period of survival of the two which died being 3 days.

Of the ten animals which were treated with echinacea one recovered and nine died, the average survival period in the fatal cases being 3.88 days, an average difference of more than eight-tenths day in favor of the treatment.

The conclusion of the authors is that "in no case did it appear that echinacea either increased the resistance of the organism to the infection or served to modify it when given as a remedy," while the average clinician in reviewing the results would be likely to claim that they showed a decided effect of the drug in prolonging the life of the infected animals.

In the series of experiments with anthrax five animals were inoculated with a suspension of *Bacillus anthracis*, two of the animals serving as controls. All of the animals died, the two controls having an average survival of 6 days, while the average survival period of the three animals receiving echinacea was only 3 days, or just half the period of survival of the untreated animals.

From the table of experiments with rattlesnake poison we learn that nine animals were given a fatal dose of venom, the dose being based upon prior experiments to determine the toxicity of the preparation. Three of the venom poisoned animals were kept as controls, while the remaining six received treatment with one or more preparations of echinacea.

The controls all died, while the animals receiving treatment with echinacea one, or 16.6 per cent. of the number, recovered. Judged by the ordinary methods of clinical deduction, therefore, the chances of recovery of animals receiving a fatal dose of rattle-

snake venom are 16.6 per cent. when treated with echinacea as compared to zero when the animals are not so treated.

From a further study of the table it is learned that the average period of survival of the controls was 2.33 days, while the average period of survival of the echinacea treated animals which died was 3 days, showing a perceptible increase in the survival period of echinacea treated animals over those untreated.

One of the authors' conclusions is that "neither of the echinacea preparations appeared to influence the course of the poisoning," but judged by the methods of deduction ordinarily employed by clinicians, it might fairly be urged that the experiments, though few in number, tend to substantiate the claim that echinacea is of value in the treatment of rattlesnake bites.

In the tuberculosis experiments a total of eight guinea-pigs were inoculated with human type tuberculosis organisms.

The control animals survived for an average period of 23 days after receiving the culture, while the average survival period of the animals receiving echinacea treatment was 31.33 days, an average increase of 8.33 days over the survival period of the untreated animals.

In the same series of experiments the progressive loss of weight of the animals inoculated with tuberculosis culture was noted. In the control animals the loss of weight prior to death averaged 202.5 gm. for each animal, while in the echinacea treated animals, though living much longer, the loss in weight prior to death averaged 156.6 gm. for each animal, or the average loss in weight of the echinacea treated animals was 45.9 gm. less than the loss in weight of those not so treated.

The authors conclude that "from these results it does not seem probable that either fluid extract echinacea or the Subculoyd Inula and Echinacea is of value in the treatment of tuberculosis," while a clinician might fairly claim that the results show a marked effect of echinacea, both in prolonging the life of the animal and in retarding the progressive loss in weight.

In the experiments with a trypanosomiasis (dourine), the guinea-pigs were inoculated with a suspension of fresh blood from rats infected with *Trypanosoma equiperdum*. All of the inoculated animals died, but while the average survival period of the controls, as shown by the table, was 51 days, the average survival period of

the animals which received echinacea was 67.16 days, or 16.16 days longer than the untreated animals.

The authors' conclusions are that "neither of these preparations appeared to influence the course of the disease. They certainly have no curative value," while a clinician in reviewing the same experiments might claim that they showed the very decided value of the drug in prolonging the lives of the infected animals.

From the foregoing it is apparent that in every series of experiments, save only those with anthrax, there was a perceptible margin of evidence, clinically speaking, in favor of echinacea treatment in the infections and intoxications experimented with, though it is possible that a restatement of all survival periods in hours instead of days might, in some of the experiments, turn the balance of the evidence in the opposite direction.

While these experiments of Couch and Giltner are perhaps too few in number to be regarded as conclusive, they are of very great value as illustrating the difference in the viewpoints and methods of deduction of the laboratory worker and of the clinician, a difference that may lead to diametrically opposed conclusions from the same observed facts.

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## POKE ROOT IN MEDICINE.\*

By U. AYLMER COATES, M.P.S.

I was very much interested in the article on *Phytolacca decandra* by our Curator, Mr. E. M. Holmes, F.L.S. (*P. J.*, November 6, page 417).<sup>1</sup> My attention was drawn to this drug some ten years since. From my own experience I have found it a very powerful alterative, and serviceable in chronic rheumatism. I have experimented with it in the form of fluid extract; it appears to be very effective in that form. From personal experience I found 3 minims of the fluid extract the best dosage. When 5 minims are taken it upsets the stomach slightly and produces emesia. Poke root is evidently a very powerful drug and worthy of further investigation. My attention was originally drawn to it by an article

\*From *Pharm. Jour. & Pharm.*, Nov. 20, 1920.

<sup>1</sup> *Amer. Journ. Pharm.*, Vol. 93 (1921), Jan., p. 47.

in a book written by Frances Peyre-Porcher, M.D., published in 1862, entitled "Resources of the Southern Fields and Forests, Medical, Economical, and Agricultural," Charleston, 1863. By command of the Surgeon-General, the author was released temporarily from service in the field and hospital to enable him to investigate into the medicinal, economical, and useful properties of plants, herbs, and drugs found within the limits of the Confederate States to enable them to be used as substitutes for drugs, medicinal substances, etc., which they were unable to obtain during the American Civil War, and the following is the account of his investigation as to the use and properties of *Phytolacca decandra*:

"The juice of the leaves or berries, inspissated in the sun to the consistence of an extract, will, it is said, discuss hard tumours if applied to the part, 'and destroy cancers by eating them out by the roots' ('Am. Herbal,' by J. Stearns). Mixed with brandy, it is extolled in the cure of rheumatism, easing pain and reducing discharge of the cutaneous and urinary secretions. One ounce of the dried root infused in a pint of wine is said to act kindly as an emetic, in doses of two tablespoonfuls. Bigelow also was of the opinion that it resembled ipecacuanha in its mode of operation; but later experimenters give an unfavourable report, as it is sometimes uncertain, acting too powerfully by accumulation. The pulverized root is also emetic in doses of one to two drachms. 'The tincture of the ripe berries seems to have acquired a well-founded reputation as a remedy in chronic and syphilitic rheumatism and for allaying syphilitic pains.' By some, thought to be more useful than guaiacum. The decoction has been used in scrofula also. A spirit distilled from the berries killed a dog in a few moments by its violent emetic effect, and, according to De Candolle, it is a powerful purgative. The French and Portuguese mixed it with their wine to give it colour, and this was prohibited by Royal Ordinance of Louis XVI 'on pain of death as it injured the flavour.' *Lind. Nat. Syst. Bot.* 210; *Mer. et de L. Dict. de M. Med.*, states that two spoonfuls of the juice of the old plant, which is acrid, will purge violently; applied externally, it will irritate the skin, and it is used in the cure of sanious ulcers, cutaneous eruptions, itch, and hemorrhoids. For the latter affection an infusion is injected per rectum. Drs. Jones and Kollock, of Georgia, assure us (adds Merat) that they cure syphilis with it, in all its stages, without the use of mercury. Dr. Rush relates that several students of Yale College were

severely purged from eating the flesh of pigeons which had fed on the berries. From the analysis in *Annal de Chimie*, lxii., 71, it is shown to contain an enormous quantity of potash—42 in 100 parts—and it is proposed to cultivate it for the manufacture of this article. From later examinations of Dr. E. Donnelly (*Am. Jour. Pharm.*, IX., 168), it appears to contain gum resin 262, starch 20, potash 2, a small quantity of fixed oil, and 66.5 of woody fibre. According to the U. S. Dispensary, it is also somewhat narcotic, and, as an emetic, is considered very slow in its operation, sometimes not acting for several hours, and then frequently upon the bowels; but the vomiting produced by it is not attended with pain or spasm. In over-doses its effects are quite dangerous. As an alternative, the dose is from one to five grains. Dr. Griffith has also used it with success in syphilitic rheumatism ('*Med. Bot.*' 535). In the supplement to the *Dict. Univ. de M. Med.*, 1846, 557, it is said to have been used with good effect in paralysis of the intestines. (*Précis des Travaux de l'Acad. de Rouen*, 188, 1838; *Comptes Rendus Hebdom. des Sci.*, lv., 12, January, 1837). The ointment, prepared by mixing one drachm of the powdered root or leaves with one ounce of lard has been applied with advantage in diseases affecting the scalp, as psora, tinea, capitis, etc. Dr. Bigelow was successful with it, and Dr. Haynard cured cases in which sulphur had failed. A gentleman informs me that he has frequently seen the sores of secondary syphilis heal up by the application of a strong decoction of the roots. Dr. Braconnot considers the yellow liquor produced by the juice of the berries one of the most delicate tests of the presence of acids. Dr. Shultz procured from half a bushel of the berries six pints of spirits, sufficiently strong to take fire and burn with readiness. The root of the plant should be dug in autumn, sliced, dried, and kept in close-stopped bottles.

"Dr. R. Moore, of Sumter District, S. C., informs me that the berries of the poke in alcohol or whisky, a dessertspoonful repeatedly given, has been found one of the most efficient remedies we possess in rheumatism. Dr. Ballard, of the same district, has used it with satisfactory results for fifty years. It is very generally employed in this way by many. The root is commonly used, applied externally, to cure mange in dogs. The root should be dug



late in autumn or during the winter, and the powder kept in close-stopped bottles, as it deteriorates.

"An excellent crimson dye is thus prepared (Thornton's So. Gardener'): To two gallons of the juice of poke berries, when they are quite ripe, add half a gallon of strong vinegar made of the wild crab-apple (ordinary vinegar will do, as the writer has seen) to dye one pound of wool, which must be washed very clean with hard soap; the wool, when wrung dry, is to be put into the vinegar and pokeberry juice, and simmered in a copper vessel for one hour; then take out the wool and let it drip awhile, and spread it in the sun. The vessel must be free from grease of any kind.

"The writer has seen articles dyed successfully with this plant during the present year (1862). The 'Solferino' colour is obtained from it. With alum to fix the colour, I have used the juice of the pokeberry as a red ink. The directions to the printer for this volume were written with this; before adding alum I found that the red colour was fugitive. I consider it, prepared as above, an excellent substitute for carmine ink."

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## DIAZO-REACTION OF MORPHINE.\*

By M. L. LAUTENSCHLAGER.

Morphine and its salts give, with diazobenzene sulphuric acid, made alkaline with sodium carbonate or sodium bicarbonate, a red coloration with increasing intensity as the quantity of the alkaloid becomes greater; a diluted acid changes the color to a yellowish orange. The reaction is yet sensitive in a solution of 1 part in 10,000. The coloring material that forms does not become fixed on the fibers in an acid bath. The reaction is not produced with the other alkaloids of opium; it can be observed neither with heroine nor with dionine, nor with peronine; none of the commoner alkaloids give an analogous coloration. The physiologic action of morphine is destroyed in the course of the reaction. This reaction can be utilized in the toxicologic search for morphine in the presence of its succedaneous or of other alkaloids.

\*Arch. d. Pharm., 1919, page 13, through *Annales de Chemie Analytique*, August, 1920, 252. V. O. H.

COCAINE AND STOVAINE, A DIFFERENTIAL  
REACTION.\*

By M. A. MANSEAU.

The chlorhydrate of cocaine and the chlorhydrate of amyleine have reactions common to all the alkaloids and particular reactions that permit of distinguishing them, some of which are given in the Codex for cocaine and in the supplement of the Codex for stovaine. Among the reactions that are common to them, there is only one that presents a special interest because it is capable of characterizing these two substances. It is the action of the weakly alkaline substances such as sodium borate, the alkaline phosphates or better, the lime water of the Codex. I have shown, in a previous note, the incompatibility which resulted in the presence of sodium borate and the chlorhydrate of cocaine in aqueous solution as an eye-wash and the advantage that there was in replacing the sodium borate by the boro-borate in order that a notable quantity of cocaine can be maintained in solution. But a very small quantity of cocaine can be, nevertheless, held in solution in the presence of sodium borate. It is not the same with stovaine. This substance is extremely sensitive to the feeble alkalies. If, indeed, there is put into a tube 1 to 12 cc of a solution of stovaine, 1 part in 1000 parts of water and there is added 1 or 2 drops of lime water, there is seen at once the precipitation of dimethyamino-dimethylethylbenzoylcarbinol. The importance of this reaction from a practical standpoint resides in the fact that the glass employed for the ampoules of stovaine should be absolutely neutral.

## DETECTION OF FORMIC ACID IN ACETIC ACID.\*

By M. POLINSKI.

WINNIPEG, CANADA.

On the basis of formic acid being easily oxidized by boiling with sulphuric-chromic acid, which does not attack acetic acid.

Twenty c. c. of the acid under examination, which should preferably contain not more than 6 to 8 per cent. of absolute acid, is mixed with 20 c. c. of concentrated sulphuric acid and 2 to 3

\**Bulletin Société de Pharmacie de Bordeaux*, 1920-3, 183. Translated by V. O. Homerberg.

\* From *The Chemist-Analyst*, April 1, 1920.

c. c. of a 50 per cent. chromic acid solution. If formic acid is present, a strong evolution of carbon dioxide takes place and green chromic sulphate is formed. Strong acids for examination should first be diluted with water in order to prevent propionic acid or other impurities present in the acid from reducing the chromic acid.

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## NEWS ITEMS AND PERSONAL NOTES

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ANNUAL MEETING OF THE AMERICAN DRUG MANUFACTURERS' ASSOCIATION.—The tenth annual meeting of the American Drug Manufacturers' Association will be held at the Hotel Biltmore, New York City, April 11th-14th. The programme announces the meeting of the Scientific Section at 10 A. M., Monday, April 11th. Three sessions of this section have been arranged. The Biological Section will hold a single session at 2 P. M. on April 11th. The meeting of the entire association will open at 2 P. M., April 12th, and sessions will be held on the 13th and 14th, and the convention will close with a banquet on the evening of the latter date.

The topics announced for discussion show that the present economic problems of the country are to receive special consideration. The question of a sales tax is to be debated, pro and con, by prominent speakers, followed by discussion by the members from the floor. The meeting bids fair to become one of the epoch-making events of the year.

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DECEASE OF GEORGE LINN VANDER VEER.—With sincere sorrow we record the decease of Mr. George Linn Vander Veer, advertising manager of the Norwich Pharmacal Company, which occurred on Friday, February 4th, at the Norwich Memorial Hospital.

Mr. Vander Veer was born in 1878 at Springfield Center, Otsego County, New York. After completing his school education he engaged as a clerk and learned the art of selling merchandise by actual experience behind the counter. Subsequently he became advertising manager for Polk & Calder Drug Company at Troy, New York. When this firm was absorbed by the Walker & Gibson Drug Company his services were secured by the Norwich Manufacturing Company, in whose behalf, as advertising manager, he has

worked zealously. About two weeks prior to his decease he was stricken with a general breakdown resulting from overwork. When pneumonia developed and his condition became serious, he was taken to the Norwich Memorial Hospital, and despite the application of the most modern medical treatment he passed away, the end coming suddenly.

The officials of the Norwich Pharmacal Company and his co-workers pay high tribute to his untiring and unselfish labors and his pleasing personality and broad knowledge.

He was not unmindful of the responsibilities of a progressive citizen and took an active interest in matters of civic welfare. He was an active member of the Episcopal Church and in the Masonic fraternity had risen to the 32d degree.

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DR. HERTY DEMANDS GERMANY'S CHEMICAL DISARMAMENT.—In an address delivered at the invitation of the National Research Council at the opening of the exhibit of the Chemical Warfare Service in the National Museum on February 21st, Dr. Charles H. Herty strongly advocated that in order to insure the peace of the world Germany should be disarmed of her supremacy in the chemical industries. He regards the dye-stuff plants of Germany as a menace to the peace of the world. He stated that their production last month of 12,000 tons of dyes was 750 tons more than the average pre-war monthly output. From these dye plants came all of the poison gases used by the German armies during the World War. He points out the danger that might result from a union of the Bolshevik Russian army of 1,500,000 men and this chemical industry, the two most powerful agencies of destruction now extant. He argued forcibly in favor of appropriations for the army and navy to continue the study of gas warfare.

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COMPETITIVE ESSAYS ON SALESMANSHIP.—In their advertisement, Colgate & Company offers a series of prizes totaling \$1500 for the best essays submitted by merchants or their salesmen on the method of displaying and selling talc. This is but another indication of the value of the training in salesmanship and evidences that it is properly made a part of the curriculum in the commercial courses in colleges of pharmacy.

It is noteworthy that while these prizes are to be awarded on

the basis of merit of competitive essays submitted by all classes of merchants, two of the judges named are Samuel C. Henry, Secretary of the National Association of Retail Druggists, and Jerry McQuade, Editor of *Drug Topics*, from which we surmise that the advertiser expects that the major portion of these essays will come from the retail drug trade.

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IMPORTATION OF ICHTHYOL NOT PROHIBITED.—A short time ago there appeared in the form of an advertising bulletin, issued by a chemical corporation, a statement to the effect that no more licenses would be granted for the importation of Ichthyol into the United States on the ground that recent investigations had disclosed that there was a similar commodity obtainable from domestic sources. In the newspapers this statement was repeated in a manner to indicate that it was a decision emanating from the War Trade Board. We are advised that this statement was misleading, and at the request of the War Trade Board a further bulletin has been issued for the purpose of correcting the false impression created by the publication of the bulletin referred to. Further, that by a decision of the Federal Trade Commission the petition of the Meadows Oil and Chemical Corporation for permission to use the name "Ichthyol" for its product was denied on the grounds that it was not in the public interest to grant such a license.

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## BOOK REVIEWS

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"THE CHEMISTRY AND ANALYSIS OF DRUGS AND MEDICINES." By HENRY C. FULLER, B. SC., in charge of the Division of Drug and Food Products, The Institute of Industrial Research, Washington, D. C. John Wiley & Sons, Inc., New York, 1072 pages. Price \$10.

In 1912, Mr. Fuller issued his first book, which was entitled "Qualitative Analysis of Medicinal Preparations." This little book of about one hundred pages has expanded in the present work to a volume of tenfold size, which is distinctive in its scope, and which will find a place in every laboratory where pharmaceutical analysis is practiced.

Its scope is comprehensive and ambitious. The accuracy and completeness of its data, up to the time of the final delivery of the manuscript to the printer, which must have been some time during 1918, are commendable.

It is divided into five general sections or parts. The first of these concerns itself with the general methods of procedure and crude drug assays. Part two covers alkaloidal drugs, alkaloids and medicinally allied substances. Part three includes glucosides, glucosidal drugs and natural drugs containing other principles than alkaloids. Part four treats of organic substances other than alkaloids and glucosides. Part five covers inorganic substances commonly found in medicines.

Under each of these headings will be found a wealth of material of interest and value to the analyst who is confronted with the problem of separating and identifying, or of quantitatively determining the substances used in medicinal preparations.

The book covers a range that no other work in the English language covers at present, and it will undoubtedly find a welcome place in reference as well as in working libraries.

There are two features of the book which could be materially improved, and it is hoped that the author will not overlook these suggestions in the future editions which are bound to appear. The first of these is in the General Methods of part 1. Here should be included much additional information concerning the analysis of such preparations as are submitted in practice. How to effect the separation of emulsions with methods for identifying the emulsifying agents or reference to the proper portion of the book for the details. How to handle ointments, plasters, mixtures and many other classes of medicinal preparations which present distinctive and difficult preliminary problems before the final separation and identification of the important constituents becomes possible. For many valuable suggestions along this line the author could have availed himself of some of the publications of the Council on Pharmacy and Chemistry of the A. Ph. A., particularly the laboratory reports, which are replete with interesting data of this kind.

The other discouraging feature is the index, which is glaringly incomplete, many substances being mentioned in the text which are not found in the index at all, some of which are of importance.

A good index to a book saves time and temper and makes the user overlook deficiencies in other respects; a poor index, however,

is a perpetual annoyance. Redundancy in this section of a book rather than paucity should be the aim, yet few but German authors know how to correctly index a book.

There are few omissions that have been noticed. Among these are the constituents of hair dye preparations, paraphenyline, diamine, henna, etc., which seem to have been given absent treatment, perhaps on the technical ground that they are not medicinal preparations in the strict sense. They, however, belong in a book of this kind naturally, and their omission will be felt by the users. The chapter on glucosidal drugs is especially to be commended for its completeness and thoroughness, although this is not intended to disparage the other sections of the book. The author is to be commended for the ambitiousness of his attempt for such books exemplify the progress of American pharmaceutical chemistry and aid in its elevation.

C. H. LAWALL.

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"INTRODUCTION TO GENERAL CHEMISTRY." An Exposition of the Principles of Modern Chemistry. By H. COPAUX; translated by HENRY LEFFMAN, A. M., M. D. P. Blakiston's Sons & Co., Philadelphia, publishers. Price, \$2.00.

This is a splendid little text book, dealing, as the sub-title indicates, with the principles of modern chemistry. It is not an introduction to general chemistry in the sense of being a book for beginners. Indeed, it is intended rather for students and for practical chemists who have mastered the elements of the science, are fairly well conversant with its nomenclature, also with its most significant facts, and are interested in viewing these facts in the light of modern theories. The book is limited in size and scope, and deals only with the basic principles, which no doubt accounts for the modest title which the author has chosen. The fundamental theories which have served as a working basis for chemists for decades are stated, discussed, and supported with laboratory evidence. But articulated with these older formulations, we find the newer hypotheses and generalizations of the science, a clear understanding of which is so necessary to the intelligent reading and appreciation of the literature of present-day chemical research.

The general style of the book is didactic rather than controversial. The opening chapter deals briefly with the conception of the

element. Then follow the laws of chemical proportions—the law of Proust, of Gay-Lussac, and of Dalton. A chapter is devoted to the atomic theory, and another to the general characters and interrelations of the elements—this including some of the more recent contributions to chemical theory, particularly along those lines which in American chemical literature are grouped under the general caption *subatomic phenomena*. Next follow the theories of solutions, a most interesting presentation, involving a discussion of dissociation, or hydrolysis, of hydrates in solutions and of solid solutions; also a rather extensive discussion of chemical affinity, touching upon speed of reactions, the law of mass action, the phase-rule, catalysis—to mention but a few of the subjects of vital interest which make up this important chapter. Then follows a brief appendix, dealing with crystal structure. And finally, there is a contribution by the translator on the subject of Hydrogen-ion Concentration, a development of the theory of ionization which has in recent years been applied in practical analysis and has made possible some very delicate quantitative work, particularly in biochemistry.

In a book of limited size one cannot expect comprehensive treatment of all chemical theories; but the selection of material—as viewed from the standpoint of American needs—is in the main a happy one. We miss, however, the generalizations pertaining to the colloidal state of matter, a subject of great interest and of practical importance. To be sure, our knowledge of colloids is in the main physical knowledge rather than chemical knowledge. But the same may be said also of much else dealt with in connection with chemical theories.

The phrasology of Dr. Leffman's translation is precise and lucid. His long experience as a teacher, and as a lecturer on chemical subjects, not only to academic classes, but also to mixed audiences, stands him in good stead in presenting the subject matter clearly. This is done, however, without any effort to avoid the technical terms of science. The principles of chemistry, it must be admitted, are inherently difficult of transmission from mind to mind; the process is not made easier, however, when it is attempted to clothe chemical abstractions in colloquial English—an attempt which usually fails, except in dealing with the simpler theories. In short, the translation is admirable in that a French text book has been rendered not in what is commonly called the King's English or the Queen's, nor in that of the kindergarten, but in English far better



adapted for the purpose, namely, the clear-cut, unambiguous English of the scientist.

It should be remembered that the book is designed to meet the needs of advanced students. And to such it may be recommended unreservedly.

J. W. STURMER.

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"PRIESTLY IN AMERICA, 1794-1804." By EDGAR F. SMITH. Publishers, P. Blakiston's Sons & Company, 1201 Walnut Street, Philadelphia, Pa.

In this sketch, covering the later period in the life of Joseph Priestly, Dr. Edgar F. Smith has woven a narrative in the interesting style that is so characteristic of this author's facile pen. In it, we get a glimpse of the real nature of the man; the humane side. The characteristics that made up his peculiar individuality are presented in a view that we have not obtained from other sketches of the life of this philosopher and chemist.

The personal touch given by the author gives us an insight into the kindly character, his philosophy, and even the false judgment and tenacious adherence to some erratic views that led him to fallacious deductions even from his own experiments. His championing of the Phlogiston theory caused him to bend his views toward explanations based thereon to the exclusion of some more obvious and scientific conclusions that have since been adopted.

Priestly appears to have been a past master in the art of controversy. His dissenting theological views and his earnestness in arguing thereon made him so unpopular in England that he became the victim of mob violence, and this was the reason for his exile to America. His friendship with Franklin probably determined his emigration.

Dr. Smith's sketch shows that, even after his arrival in America, his life was not free from this disposition to controversy. His views called forth remorseless attack from William Cobbett (Peter Porcupine), whose abusive and sarcastic productions were a feature of the literature of that decade.

The events associated with Priestly's landing in New York and the various addresses of welcome show that he was given quite an ovation upon his arrival in the new country.

In the fall of 1794, Priestly took up his residence in North-

unberland, Pa. The close proximity of his residence to Philadelphia permitted him to make occasional visits to the city and to associate with the scientific men of Philadelphia of that period, and form many lasting friendships with these. His several contributions to the American Philosophical Society are referred to, and the events in his personal history are feelingly described.

In perusing the pages of this book, one is convinced that Joseph Priestly played an important part, during his sojourn in America in the last ten years of his life, by his discussions not only on chemical subjects but on political, theological and educational matters, and withal science, as he understood it, was interwoven.

In this publication, the author has added another service to the many that he has rendered in behalf of chemical sciences, by reciting reminiscences of the later days, and giving us a clear view of the events associated with the career and life of Joseph Priestly. The epitaph on his tomb stone in the Northumberland burial ground is peculiarly appropriate to the character of one whom we must consider as a foremost philosopher of his day.

“Return unto thy rest, O my soul, for the  
Lord hath dealt bountifully with thee.  
I will lay me down in peace and sleep till  
I wake in the morning of the resurrection.”

G. M. B.

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“A CRITICAL REVISION OF THE GENUS EUCALYPTUS.” By J. H. MAIDEN, I. S. O., F. R. S., F. L. S. Vol. V. No. 3.

Part XLIII of this complete work, now in hand, continues this classical study of this genus of plants so important to Australia from both a botanical and economical viewpoint. The uniform plan of treatment of the subjects, adopted in the preceding parts of this work, are continued in the present section. In this the following species are considered: *Eucalyptus ficifolia* F. v. M.; *E. calophylla* R. Br.; *E. hamatoxylon* Maiden; *E. maculata* Hook; *E. Mooreana* (W. V. Fitzgerald) Maiden; *E. approximans* Maiden, and *E. Stowardi* Maiden.

The four plates in this part maintain fully the high artistic illustrations that are characteristic of this monographic study.

G. M. B.

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## EDITORIAL

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### TREATMENT OF BICHLORIDE OF MERCURY POISONING.

Physicians have frequently asserted that the symptomatology of bichloride of mercury poisoning is as diversified as that of the dreaded lues. And they likewise state that in view of these varying symptoms treatment must synchronously vary.

For many decades the legend on the label of the bichloride tablet bottle has called for administering to those who have indulged in the vicious drug some white of egg, or egg albumen. Often there is established a specific ratio between the amount of albumen and poison, but more frequently one finds a random statement in regard to the amount of albumen which shall be given. The stomach pump and gastric lavage have likewise been much used in connection with antidoting this poison. But generally the results were not good, and this despite the sound theory of stomach washing.

The futility of all these measures undoubtedly lies in the fact that there is very rapid absorption of this poison, and that local measures of antidoting come too late. It is stated that even within fifteen minutes there is very little uncombined bichloride of mercury left in the stomach. And still another fact that denotes the weakness of our past mode of treatment is to recall that the insoluble albuminate of mercury, formed when the white of egg binds itself with the poison, is soluble in the presence of an excess of the albumen. Because of this fact there is never a degree of certainty attached to the chemical antidoting with albumen, for the physician seldom knows how much bichloride of mercury the patient has taken, and *never* knows what quantity remains in the stomach at the time of treatment.

It is important that pharmacists inquire into the newer ideas in regard to this question, and we take the privilege of quoting the following statements from an editorial article which recently appeared in the *Hahnemannian Monthly*:

"Of late years calcium sulphide has been recommended as a bichloride antidote. This agent coming in contact with the bichloride solution produces an insoluble sulphide of mercury and no excess of antidote is capable of re-dissolving the precipitate, hence it should prove to be an efficient antidote; the objection to it, however, is that by the time it is introduced into the stomach the latter organ is empty and any antidotal influence of calcium sulphide depends upon its absorption into the circulation.

"About three years ago J. H. Willus, of Cincinnati, made some elaborate experiments covering this subject, published in the *Journal of Clinical and Laboratory Medicine*. This plan of treatment is beautifully simple, so simple indeed that the physician is only too likely to make efforts at improving it or making it look complicated; thus defeating his purpose. Its very simplicity is a testimonial to its efficiency. Of the last fourteen cases of poisoning treated at Hahnemann Hospital but one patient died, and that one took over 140 grains. One patient who recovered had taken 49 grains. Of those who recovered not one had nephritis.

"The treatment as carried out was this: An intravenous administration of sulphide calcium in the proportion of one grain to the ounce in sterile water was employed promptly on the admission of the patient. The total quantity of calcium sulphide used was one grain for every grain of bichloride supposed to have been taken. The main care in the preparation of the sulphide solution was the avoidance of small particles of calcium sulphide held in suspension and not evenly enough divided. These can very readily be taken out by passing through some loosely packed absorbent cotton in a filter. Following the intravenous, the patient is given one grain of calcium sulphide, sometimes more, by the mouth every hour for several days. Such is the treatment.

"No attempt should be made to mix the sulphide with normal saline solution, as such most unquestionably would interfere with the chemical reaction. No time should be lost by preliminary washing out of the stomach. No attempt should be made to add any details which the imagination or ingenuity of the physician may suggest. It is simply a question of getting sufficient calcium sulphide into the circulation as quickly as possible."

The foregoing plan is exceedingly simple and apparently productive of unusual results. The pharmacist whose duty it will be to prepare this solution for intravenous medication, will mark well

the care which must be exercised in dispensing only a clear solution, *absolutely* free of suspended material of any nature. The calcium sulphide used shall also be of the highest available purity and solution effected not in sterile salt solution, but in sterile distilled water.

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"BOOKS IN RUNNING BROOKS, SERMONS IN STONES  
AND GOOD IN EVERYTHING."

So wrote one whose understanding and love of nature was intense and true. This day of writing is a bright day in spring, early in April, when the robin ushers in the morning with his chant of hope and happiness. And we look out through the window-pane on a country-side yawning itself out of its winter's slumbers and garbed in the verdant hues, the fresh and lively greens of early spring.

Weary with the arduous tasks of a long and dreary winter that has kept us out of the fields and the bypaths where we love to wander, spring comes, doubly welcomed. The newness of it and the hopefulness of it fills us with delight and the siren-song of the woods quickly finds its responsive chords in the tune of the heart strings that bids us forget our labors awhile and seek again the re-creation the rejuvenation which promptly comes to us with spring.

So we leave behind our troubles and forget awhile the pilltile and pestle, the filter and funnel, and to the woods through the meadows we go.

What a happy thought, were it possible and convenient for every man (and who can appreciate this better than the busy apothecary) to find time to let work alone for awhile and turn his footsteps to the nearest woods to seek communion with the trees and flowers. For it is said, and truly said, that the road to Divine understanding is plainly told in the face of every flower.

Early in the morning, when the glistening dew drops nestle in that plaitain and bend the grass blades with their jewelled night, that is the time when the searcher after peace and beauty can find his fill of nature's choicest charms.

Sustained by the sun of early April filtering his healthful rays through a screen of ambitious beech buds, the cozy knobs of hepatica and bloodroot unfold their precious contents and shortly their dainty blossoms stare with complacency straight in the eye of the

sun. The mandrake in festive colonies marks the country-side and under rustlings noisy leaves of beech and oak left dead from last November, a tardy *Arbutis* pushes its fragrant blossoms also eager to find its place in the spring sun.

And the pilgrim to nature's shrine finds beauty in them all.

To the materialist it is perhaps a long, long road from the twisted ugly root of *sanguinaria* which he grinds in the mill and packs in the percolator, to the stately and pure flower that towers over its blood-red reservoir in the spring woods. And the charming May-bloom that modestly hides its beauty beneath a canopy of green leaves is likewise far removed from the ancient, ridged roots and rhizomes of *podophyllum peltatum* that fills a can in the store-room.

But the heart of the real apothecary-man is surely gladdened to know that he is privileged over all other men in his understanding of these common members of God's great kingdom.

"Books in Running Brooks, Sermons in Stones"—and even more than all of these in Flowers. Harken to the story of the flower and you hear a tale that sounds strangely alike to the story of your life and mine. How naturally they adapt themselves to their environment, give their offspring a healthy start in life's long journey. How they settle new colonies in far-off land; their co-operative methods; their storage of treasure against possible droughts. These have been the ways of the flowers for many centuries, and we can humbly take a lesson from them.

Brothers in back of the counter, in the warehouse or at the desk; Sisters in the Hospital drug room or laboratory—seek ye new courage and inspirations, new hopes and thoughts? Then hie to the woods and meadows where all of these attributes and all of these blessings wait for the mere calling of them.

## ORIGINAL PAPERS

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### HYBRIDIZATION IN PLANTS.\*

By HEBER W. YOUNGKEN, Ph.D.,

PHILADELPHIA, PA.

The term *hybrid* is a derivative of the Greek word, *ὑβρις*, an outrage or insult, and a hybrid was regarded by many of our ancestors as an outrage on nature.

Hybridization, according to older definitions, was defined as the intercrossing of two recognizably different species, the resulting product being therefore spoken of as a *hybrid*. The term *mongrel* was applied to the crossing of two varieties of the same species; but so many graded connections between the two have been shown to exist that the term "hybrid" now exists in common use to cover every case.

In thinking of degrees of similarity or difference between parent forms in relation to their offspring, it is well to bear in mind that diverse types of plants in many respects may characterize members of the same species. Thus, the staminate plants of *Lychnis vespertina* and *Lychnis diurna* differ markedly from the pistillate plants in height, vigor and thickness of stem and in hairness and size of leaves, apart from the doecious sexual relation.

Again, dimorphic plants like the primroses and partridge berry and trimorphic plants like the purple loosestrife, while usually resembling each other in vegetative parts, differ strikingly in the structure of androecium and gynoecium.

Moreover, in the genus *Catasetum* of the *Orchidaceæ*, plants sent successively from South America, were described when they flowered as three genera under the names "*Catasetum*," "*Monacantha*," and "*Myanthus*." In time it was shown that the totally distinct forms of flower represented staminate, pistillate and hermaphrodite examples of the same species.

In considering possible hybridization and the degree of resemblance and difference shown by parents, such facts as mentioned

\*Philadelphia College of Pharmacy and Science, January 31, 1921.

that illustrate individual variation in a species should be kept in mind.

Regarding the possibility of crossing between distinct varieties, species or genera, it might be said that hybridization seems in many cases easy between varieties, sometimes easy and at other times difficult between species and only rarely possible between genera. When the last is accomplished, the progeny is spoken of as a bi-generic hybrid.

Apparent obstacles, however, to crossing even varieties seem at times to exist. Thus, colors of diverse kinds may form a strong barrier. As first pointed out by Charles Darwin, the scarlet pimpernel (*Anagallis arvensis*) may grow in abundance with the blue pimpernel (*Anagallis caerulea*), the former with bright scarlet, the latter with azure blue flowers, but both in the wild state and under cultivation hybridization seems difficult. But that crossing may be effected is shown by the ugly, lurid garden progeny, *Anagallis Phœnicia*.

Similarly, a cross between the scarlet cardinal flower (*Lobelia cardinalis*) and the blue *Lobelia siphilitica* is extremely rare in the wild state, and, when secured under cultivation, the flowers of the hybrid possess a lurid, ugly, pinkish purple color. In this instance the intermixture of deep orange pigment in the cell chromoplastids with dissolved alkaline blue pigment is a semi-incompatible condition.

Again, hybridizers have often observed that some families contain species that cross readily while other families seldom hybridize. Of the former it seems generally the case, that when the family includes regular and irregular flowered genera, the former cross with difficulty, the latter with ease. For example, in the Geranium family, *Geranium* and *Erodium* fail to cross in their species, while *Pelargonium* crosses very readily.

Again, *Rhododendron* and *Azalea* species with irregular flowers cross readily, while crosses between regular flowered members of the Heath Family are rare.

Crosses between even diverse looking species of a genus may often be effected with ease and the hybrid progeny often blends the characters of both parents in even numbers. Thus *Verbascum*, *Dianthus*, *Pelargonium*, *Sarracenia*, *Nepenthes* and many others blend readily even between the most diverse species and the progeny is largely fertile.

Crosses between genera have only rarely been effected and



mainly amongst such Monocotyledonous families as *Liliaceae* and *Orchidaceae*. When effected, the hybrid progeny is often designated by a compound generic term. Thus, in the crossing of the Liliaceous genus *Philesia* with the genus *Lapageria* of the same family, the resulting hybrid is known as *Philegeria*. Similarly in the crossing of the Orchids *Lattia* and *Catleya*, the resulting hybrids are known as *Laeliocattleya*.

Where the parent forms have been highly cultivated and gradually modified by man for years or centuries, the resulting progeny often becomes mixed and correspondingly unstable. One result of this has been that our most abundant garden flowering plants of the present day are hybrids of extremely mixed type and often doubtful parentage, as in garden pinks, petunias, tobaccos, fuchsias, cresses and others. These all tend from their blended parentage to vary or sway in irregular and often fortuitous manner. Such is also true regarding many cultivated varieties of a single species, e. g., peas, beans, apples, peaches, potatoes and tomatoes.

In the crossing of varieties and species it may be said broadly that the hybrid produces the characters of the parents in blended manner but reduced by about one-half the minutest cell details shown by both, when these are capable of blending. Where certain histological details in one parent are alone present and absent in the other parent, such may appear in the hybrid but reduced about one-half. For example, the sepal of *Philesia* is devoid of a nectar gland, while the sepal of *Lapageria* has a large nectar gland. When these species are crossed *Philegeria*, the hybrid, shows sepals, each of which is found to possess a nectar gland one-half the size of that of the *Lapageria* parent.

Again, if both species develop diverse histological details, these may be reproduced side by side in the hybrid, but each reduced by about one-half. Thus, Gooseberry leaf epidermis bears long unicellular non-glandular hairs. Black Currant leaf epidermis is devoid of these, but has volatile oil glands. In the hybrid between these the unicellular hairs and the volatile oil glands are reproduced, but each reduced by about one-half.

Similarly, the leaves of *Myrica cerifera* possess numerous golden-yellow, balloon-shaped glands and orange-red bowl-shaped glands and few non-glandular hairs on both epidermises. The leaves of *Myrica Carolinensis* show numerous golden-yellow, balloon-shaped glands on the lower epidermis and few or none of these on the upper epidermis, while numerous non-glandular hairs

appear on both epidermises. The leaves of hybrids (*M. cerifera* x *M. Carolinensis*) show numerous orange-red, bowl-shaped and golden-yellow, balloon-shaped glands on the lower epidermis, but often fewer than on the similar epidermis of *M. cerifera*. The upper epidermis shows a scattering of orange-red, bowl-shaped glands and golden-yellow, balloon-shaped glands, while the number of non-glandular hairs on both epidermises are fewer than on *M. Carolinensis* and more numerous than on *M. cerifera*. The tendency for the head of the bowl-shaped gland in the hybrid to become saucer-shaped is very striking.

Further, as to hardness of hybrids in relation to parents, the hybrid is very evenly intermediate between the two parent species. For instance, our Mountain Rhododendron (*Rhododendron maximum*) resistant to frost, when crossed by the scarlet Himalaya Rhododendron (*Rhododendron arboreum*) tender to frost, gives a hybrid that will resist 15 deg. to 20 deg. above zero.

Again, in the case of the Myricas, the leaves of *Myrica cerifera* (Wax Myrtle) are evergreen and remain green on the stems over winter until late April and early May without assuming a coppery color. Those of *Myrica Carolinensis* (Bayberry) are deciduous, assuming a greenish-brown hue in October and November and usually completely fallen by the middle of December, while the leaves of hybrids between these two parents are semi-evergreen and usually fall in February and March, by which time they have often assumed a slight coppery tint.

The plant breeder, in starting any work in hybridization, is obliged to choose the varieties or species to be hybridized. He must have some definite aim in view. He must study his plants and determine their good and weak characters. These characters may be tallness, dwarfness, high or low percentage of active constituents, color of leaves, flowers, or other organs, hairiness or smoothness, starch or sugar content of seeds, etc. He must then use his judgment in deciding what combinations of these characters would form the best variety.

Unfortunately the reaction between different characters or factors on one another in various combinations has not always been what was expected. Up to the present, the followers of the Mendelian theory have been unable to make a complete analysis of all the unit characters or factors in any plant with which they have worked. While they are generally able to predict what will happen when pure strains or varieties of plants, having up to five pairs of

contrasted unit characters are crossed, nevertheless, when they take into consideration a multiplicity of factors, there are discrepancies in the working out of the theory which remains unexplained to the satisfaction of geneticists.

There is, accordingly, always an element of doubt as to what the results of a new cross may be, until the combination has been produced and tested.

#### METHODS OF CROSSING PLANTS.

In the majority of instances among Spermatophytes, the plants bear flowers having both male reproductive organs (stamens) and female reproductive organs (carpels) in the same bloom. In some cases, as in the genera *Zea*, *Croton*, *Ricinus*, *Pinus*, *Castanea* and *Quercus*, both of these sets of essential organs are borne on the same plant, but in different flowers. In still others, as the genera *Cannabis*, *Humulus*, *Salix*, *Populus*, etc., the stamens and carpels are borne in flowers of different plants of the same species.

In the practice of crossing, care must be exercised to the end that plants are not fertilized with their own pollen or with pollen from any other than the desired source. Accordingly, if the plant to be hybridized has the stamens and carpels in the same flower, as for examples, Aconite or Larkspur plants, the stamens must be removed from the flower in the bud condition, before the anthers have burst and discharged their pollen. This act is known as "emasculatation" and is absolutely essential in order to prevent self-fertilization. In protandrous plants, *e. g.*, those with flowers in which the stamens elongate and mature their pollen before the ripening of the carpels, it is necessary to emasculate the buds quite early, while in protogynous plants, *e. g.*, those with flowers in which the carpels mature before the stamens, emasculatation can be deferred until just before the opening of the flower bud.

In all cases where petals are found in the floral make-up, these are either pried apart or cut away. The stamens are pulled out by forceps, care being taken not to injure the pistil. The bud is then enclosed in a paper bag in order to prevent pollen from any other source being brought to the pistil. After waiting a sufficient length of time to allow the pistil to reach maturity, the paper bag is removed and pollen from the desired variety dusted on the pistil. The bud is again covered with the paper bag and allowed to remain for several days or longer until fertilization has taken place. A labelled tag, indicating the nature of the cross, is then tied by fine

copper wire, preferably, to the flower-stalk, until the fruit is mature.

When the seeds of this fruit are planted they germinate and grow into adult plants that possess characteristics partly resembling one parent, partly the other. These are termed first generation hybrids. Seeds collected from these hybrids give rise to second generation hybrids, and those from the latter originate hybrids of the third generation.

It is surprising that so little work has been done up to the present on the hybridization and selection of varieties of medicinal plants to the end that staple hybrids may be procured, yielding a higher percentage of active constituents than the presently known plants. If hybridization as applied to varieties of Cinchona plants has resulted in doubling the yield of alkaloidal principles over the amount found in mossed barks, it is not logical to assume that its application to many other drug plants would offer wonderful possibilities in improving their quality and therapeutic efficiency?

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## ABSTRACTED AND REPRINTED ARTICLES

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### STUDIES ON PEPSIN.\*

By LEWIS DAVIS AND HARVEY M. MERKER.

*Chemical Changes in the Purification of Pepsin.*

The question of the chemical composition of pepsin has occupied the attention of a number of investigators. Following the classical researches of Pawlow and his pupils, Pekelharig appears to have been the first to undertake purification of the enzyme. This investigator prepared a light yellow powder which, while readily soluble in dilute acids and sodium chloride solution, dissolved with difficulty in water but showed strong peptic activity. It gave reactions for albumin, but was believed to contain a soluble phosphorus compound as an impurity. On boiling pepsin solutions, Pekelharig

\*Contributions from the Research Laboratory and the Department of Glandular Extracts, Parke, Davis & Co. Reprinted from *Pure Products*, February, 1921.

obtained a nucleo proteid and was able, under certain conditions, to separate an albumose.

Nencki and Sieber, using as initial material juice obtained through gastric fistula in dogs, claim to have secured an active pepsin preparation through precipitation which is free from albumin. At the same time, they consider the precipitate of transparent granules containing chlorine which they obtained by strongly cooling the gastric juice to be a chemical individual, and, in all probability, the true enzyme. They also submit analyses to support their contentions. Pekelharing, in a later investigation, in which he employed the artificial juices extracted from several hundred hog stomachs by his previous method, and also the juice obtained from gastric fistula in dogs, disproved this view. He found pepsin to be free from phosphorus and to contain no nucleo proteid, but the analyses of his preparations showed no constancy in results.

That a protein-free pepsin solution having digestive action is possible, has also been maintained by Schrumph. The latter prepared a Büchner-pressed extract of hog stomachs, clarified by filtration, and dialyzed against running water. The dialysate thus obtained was precipitated by addition of cholesterin in alcohol-ether solution, filtered, the precipitate redissolved in water, and the suspension finally clarified by a Kitasato candle. The clear filtrate, while giving none of the protein reactions, still showed powerful digestive activity.

The amino acid constituents of pepsin have been investigated by Hugounenq and Morel using an autodigested, hydrochloric extract of hog stomachs. They conclude that an extract of pepsin contains a number of monoamino acids in the free state, probably formed in the autodigestion. Glycocoll, aspartic and glutaminic acids, and also histidin, they found to be absent in the material examined.

It is thus readily apparent that, as true with other enzymes, the chemical nature of pepsin is still an open question. Nearly all of the above investigators have based their conclusions on crude preparations, undoubtedly containing admixed or combined impurities. Seemingly, no attempt has been made to prove, by quantitative measurements of the proteolytic activity, that an actual purification has taken place, where such is mentioned. The present investigation was undertaken by us to determine what changes take place in the purification of pepsin, with the view of possibly throwing some light on the chemical nature of the enzyme.

## EXPERIMENTAL PROCEDURE.

*Methods.*—As basic material for purification, a composite lot (consisting of a number of different samples) of 1 :2000 commercial pepsin was employed. Sufficient stock of this mixture was reserved to enable the preparation of all of the various strengths of the enzyme given below. The weaker samples (up to 1 :18000) were prepared by fractional precipitation of a 20 per cent. aqueous solution, while the more active strengths were obtained by salting out the former, filtering and dialyzing. In each case, the final purified material was dried to a constant moisture content of about 5 per cent. and sealed. Assays for proteolytic power were then carried through and the samples analyzed chemically.

Determination of the proteolytic strength of the different samples, made in association with our colleagues, L. M. Gerdes and W. L. Seibert, was in accordance with the method given in the 9th revision of the U. S. Pharmacopœia. The assays were checked in each case, and controlled by running through a standard (1 :3000) pepsin under identical conditions.

The chemical examination included analyses of total mineral matter, total nitrogen, total sulphur by the method of Wolf and Osterberg, volumetric estimation, in the ash, of phosphoric acid as  $P_2O_5$ , chlorides as NaCl, calcium as  $CaCO_3$ ; also, determination of nitrogen existing in coagulable protein, proteoses by zinc precipitation, peptones by Bigelow and Cook's modification of Sjerning's method, and amino acids according to Van Slyke. In addition, observations were made in a 2 per cent. aqueous solution of optical rotation, and of the hydrogen-ion concentration. The direct reading ionometer described by Bartell was used in the latter, with a Weston Standard Cell, and the chain: Calomel electrode (NKCl)—saturated KCl—pepsin solution—Pt electrode— $H_2$  at 23 degrees. The complete "set up" employed was similar to that used by Davis in a previous investigation of diphtheria toxin.

Supplementing the preceding, qualitative tests were carried out in accordance with the technique employed by one of us, Davis, with peptone samples. Both a straight 2 per cent. aqueous solution and the filtrate, after coagulating the protein, were used, and examination made for: tyrosin (xanthoproteic, Millon's reaction) tryptophane (Adamkiewicz Hopkins-Cole reagent), glycoprotein and glycoproteose (Molisch reagent). Tests were also made on the filtrate from coagulable protein, for proteoses (by addition of satu-

rated zinc sulphate, ammonium sulphate, picric acid solutions), and protoproteoses (by saturated sodium chloride solution, potassium ferrocyanide in acetic acid solution).

*Results.*—Altogether, nine purified products were prepared. Including the basic pepsin material, the various proteolytic strengths of the enzyme which were examined ranged from 1 : 2000 to 1 : 40,000 (U. S. P. IX). The results in every case, based on duplicate determinations and, because of possible variation in the U. S. P. pepsin assay, these estimations were carried out in triplicate by two different observers.

The purification of pepsin is accompanied by a general decrease in the total mineral matter. This ranges from an ash content of nearly 5.5 per cent. in the case of the basic (1 : 2000) product down to about 2 per cent. with the highest proteolytic strengths obtained. The phosphoric acid content, also, shows a gradual decrease so that the value at 1 : 40,000 is less than one-third that of the basic material. Both the calcium oxide and total sulphur values fluctuate in the different strengths, but both show an increase in the purified as compared with the unpurified samples. It is a significant fact that the chlorides, which are present to the extent of 1.19 per cent. (as NaCl) in the 1 : 2000 sample, practically disappear as a result of purification.

Probably the most important data are furnished by the various nitrogen factors, particularly the nitrogen in amino acid condition. Confirming more elaborately the results found by other investigators, there is found to be almost a uniform decrease in  $\alpha$ -amino acid nitrogen so that in the sample testing 1 : 40,000 only 0.61 is found. Corroborating these results, it will be noted that there are steady increases in both the coagulable protein nitrogen and that existing as proteoses, while the peptone nitrogen like that of the amino acids shows a decrease. The values for total nitrogen showed decided variations among the different samples with no significant change as the purification increases.

All of the different strengths of the pepsin examined show levorotation in very nearly the same degree, so that this factor is apparently unaltered as a result of purification. With the exception of the strongest sample obtained (1 : 40,000) a slight amount of hydrochloric acid was used in the preparation of the other strengths of the pepsin. As a consequence, 2 per cent. aqueous

solutions of these samples show relatively high hydrogen ion concentration. However, the reaction of the 1 : 40,000 sample, which is the nearest approach to the pure enzyme, is very nearly neutral ( $\text{PH} + = 6.0 \times 10^{-7}$ ). This would tend to disprove the view held by Jacoby and others that pepsin is an acid.

No tests were made on the straight pepsin solutions with saturated picric acid, sodium chloride and ammonium sulphate solutions, and also none with potassium ferrocyanide in acetic acid solution, since the results with all of these reagents, because of coagulable protein would be positive, and practically the same for the different strengths. The saturated picric acid, Hopkins-Cole, and Millon's reagent tests, which were made of the filtrate after removal of coagulable protein, show presence of amino acid and peptid bodies in the lower strength samples. These gradually disappear so that only traces are found in the highest strength sample of the enzyme. Both saturated sodium chloride solution and potassium ferrocyanide in acetic acid solution gave negative results, indicating absence of protoproteoses in the filtrate from coagulable protein. A positive reaction was obtained in every case with Molisch reagent showing presence of glycoprotein, or its derivatives, in the material. It is significant that the biuret test of the filtrate after coagulation of protein in the 1 : 40,000 sample, is negative. This would indicate that practically all of the protein material is of the nature of coagulable protein or even more complex in its protein character.

#### DISCUSSION.

A review of the data presented in the foregoing seems to show that in the purification of pepsin there is a gradual elimination of the secondary protein derivatives including amino acids. This is manifested by a constant tendency in the purified samples to approach nearer to the actual character of proteins with increasing proteolytic activity, and is accompanied by an increase in material coagulable by heat. From the fact that the highest strength samples still give strong tests with Molisch reagent, it may be possible that the pure enzyme is a conjugated protein, probably a glycoprotein.

Confirming this view, the mineral matter is decidedly less in the purified samples than in the original basic material, approaching almost to the value for pure proteins in the case of the strongest samples. Both sulphur and calcium are probably unaffected by the



purification, but there is a decided decrease in the phosphorus content and seemingly a total elimination of chlorides. Other than the increase which would obtain by removal of non-nitrogenous impurities, there is probably not much change in the content of total nitrogen as a result of pepsin purification.

The manner in which the *α*-amino acids decrease as the proteolytic activity increases is striking, and seems to be almost proportional in amount. It is noteworthy that the small amount of *α*-amino acid present in the sample testing 1 : 40,000 (0.61 per cent.) very nearly approaches the value for this factor due to lysin as found present by Van Slyke and Birchard in most proteins analyzed by the nitrous acid method.

Results of optical activity determinations are apparently of no significance, since the same values are obtained with several different strengths of pepsin. As already mentioned above, the reaction in aqueous solution of the strongest (1 : 40,000) pepsin is significant because of its very slight acidity. It would seem very likely, that the concentration of hydrogen ions in solutions of the pure enzyme, when isolated, will probably show only the slight acidity comparable to that given by other proteins.

In connection with the assays of proteolytic strength by the U. S. P. method, it was deemed of interest to make a comparison of the rennetic power of the different samples. It is a significant fact that throughout the entire series, from 1 : 2000 to 1 : 40,000, the rennetic activity and proteolytic strengths are found to go hand in hand.

#### CONCLUSIONS.

1. The purification of pepsin seems to consist in the elimination of secondary protein derivatives including *α*-amino acids.

2. Calcium and sulphur appear to be unaltered as a result of purification, but phosphorus is materially reduced. Chlorides are seemingly entirely removed.

3. Aqueous solutions of pepsin, after purification, show no material change in optical activity. A sample of high digestive power (1 : 40,000), shows a reaction very nearly neutral.

4. Pepsin tends to approach nearer to the actual character of a protein (possibly a glycoprotein) with increasing proteolytic activity.

THE DEGREE OF SWEETNESS OF DULCIN <sup>1</sup> AND OF SACCHARIN.\*

By PROF. DR. THEODOR PAUL.

Saccharin is usually rated as about 450 and dulcin 250 times as sweet as sugar. By the addition of dulcin to a solution of saccharin the increase in sweetness is much more than that corresponding to the additional sweetness derived from the added dulcin. For instance, the sweet taste of a solution containing 280 mg. saccharin per liter is raised by the addition of only 120 mg. of dulcin to the same degree as a solution of 535 mg. of saccharin in a liter. The sweetness is thus almost doubled and also a saving of 33 per cent. of sweetener achieved.

This phenomenon is explained by the observed fact that the "coefficient" of sweetness of saccharin and of dulcin is greater in dilute solution than in more concentrated. For saccharin it varies from 200 to 700 (compared with 210 per cent. sugar solutions) and for dulcin from 70 to 350. In the instance cited above, the degree of sweetness of 280 mg. saccharin in a liter corresponds to a 7 per cent. sugar solution and that of 120 mg. of dulcin to a 3 per cent. sugar solution. The sum of the two corresponds to a 10 per cent. sugar solution, whereas to produce the same degree of sweetness by the use of either saccharin or dulcin alone, 535 mg. of the former or 1430 mg. of the latter is required.

The following table shows the quantities of the different sweeteners required to make a solution possessing the same degree of sweetness, sugar (saccharose) being taken as the standard for or of dulcin, and column 4 represents the quantities of saccharin and of dulcin required to match the sugar solution in column 1. comparison. Columns 2 and 3 represent the quantities of saccharin

<sup>1</sup> Dulcin, or para-phenetole carbamide,  $\text{NH}_2\text{CO} \cdot \text{NH} \cdot \text{C}_6\text{H}_4 \cdot (\text{O} \cdot \text{C}_2\text{H}_5)_2$ , forms colorless or slightly yellow needles, soluble in about 800 parts of cold water and in about 50 parts of boiling water. It is obtained by the action of phosgene on para-phenetidine and treatment of the resulting chlor compound with ammonia.

\*Reprinted from *Chem. Zeit.*, 1921, No. 4. Abstracted by Joseph Rosin.

*Isodulceous Solutions, i. e., Solutions Possessing the Same Degree of Sweetness.*

1	2	3	4	5
Sugar	Saccharin	Dulcin	Saccharin & Dulcin	Sum. of Sach. & Dulcin
Gm. in 1 Lit.	Mg. in 1 Lit.	Mg. in 1 Lit.	Mg. in 1 Lit.	Mg. in 1 Lit.
10	20	30	..	..
20	30	55	..	..
30	55	120	..	..
40	100	290	55	30
50	150	480	55	55
60	190	665	100	55
70	280	855	150	55
80	370	1050	190	55
90	450	1250	190	120
100	535	1430	280	120

Of added interest is the observation that the sweet taste of solutions containing saccharin and dulcin is *more agreeable* than that of a solution of saccharin alone.

## A NEW SOURCE OF SANTONIN.\*

By HENRY G. GREENISH AND CONSTANCE E. PEARSON.

A few weeks ago a small quantity of the leaves of a species of *Artemisia* was referred to the Pharmacy Research Laboratory for identification and for examination, more particularly for the possible presence of santonin. The material consisted almost entirely of very hairy, much sub-divided leaves. They were identified at the herbarium of the Royal Botanic Gardens, Kew, as being derived from *Artemisia brevifolia*, Wallich. This plant is described by Hooker,<sup>1</sup> under the name of *A. maritima*, Linn., and the following details are taken from his description: The plant produces a woody, branched rootstock with woody or wiry stems, 6 to 18 inches high, erect or ascending and much branched from the bases. The leaves are half to two inches long, ovate, 2-pinnatisect, often quite white, with very many small, spreading, linear, obtuse seg-

\*Contribution from the Pharmacy Research Laboratory of the Pharmaceutical Society. Reprinted from the *Pharm. Jour. and Pharmacist*, January 1, 1921.

<sup>1</sup>*Flora Indica*, Vol. iii, p. 322.

ments, the whole plant being hoary and tomentose. The flower heads, often reddish and crowned, are 3- to 8-flowered, ovoid or oblong, suberect, in spicate fascicles; involucre bracts linear-oblong, the outer herbaceous, tomentose, the inner scarious, acute and glabrous. It occurs from Kashnir to Kumaon at an altitude of 7000 to 9000 feet, and in Western Thibet is abundant at an altitude of 9000 to 14,000 feet. The plant appears, therefore, to be distributed over a very wide area, and to occur in some abundance.

A preliminary experiment having shown the presence of a crystalline substance resembling santonin, 100 Gms. of the material were divided into two portions, and each portion extracted in a Soxhlet with chloroform for two hours.<sup>2</sup> The chloroformic solutions were mixed and the chloroform distilled off on a water-bath until about 10 Gms. were left. To this about 250 Gms. of a saturated aqueous solution of barium hydroxide were added and the flask again heated on the water-bath until all the chloroform was driven off. The liquid was then filtered and the filter washed with a little boiling water. The filtrate was acidified with 15 Gms. of hydrochloric acid (containing 25 per cent. of HCl), heated on a water-bath for a few minutes, and, when lukewarm, transferred to a large separator. The flask was rinsed with 40 c. c. of chloroform, which was transferred to the separator and the whole shaken for two minutes. After separation the chloroform was drawn off and the operation repeated with two more successive quantities of 40 c. c. chloroform. The united chloroformic solutions were distilled to dryness, the residue dissolved by the aid of heat in 15 c. c. of absolute alcohol, and 85 Gms. of hot distilled water added. The milky solution was immediately filtered into a tared Erlenmeyer flask and the residue on the filter washed with a little diluted alcohol. Crystals, however, had separated during filtration, and the residue on the filter paper was therefore dried, redissolved in absolute alcohol, hot distilled water added, and filtered as before. After 24 hours the crystals that had separated were collected on a tared filter paper, the flasks were rinsed with 20 c. c. of a mixture of 3 Gms. of absolute alcohol and 17 Gms. of distilled water, which

<sup>2</sup> See "Year-Book of Pharmacy, 1914," p. 138.

was then used to wash the filters. After drying, both flasks and filters were weighed. The total amount of crystals thus obtained was 0.85 Gm. They were slightly brownish in color, and were purified by recrystallizing from diluted alcohol and decolorizing with a little animal charcoal; they were then quite colorless. Dried at 100°, they melted at 170°, which is the melting-point of santonin. A mixture of the crystals with commercial santonin melted at 169.50°. Warmed with alcoholic potash, a violet solution was obtained. A little warmed in a water-bath, with 5 c. c. of a mixture of equal volumes of sulphuric acid and water, to which a trace of ferric chloride had been added, gave a yellow color and slowly passing to orange, red, violet, and lavender. These two color reactions are characteristic of santonin, and taken in conjunction with the melting-point, leave no doubt that the crystalline substance is santonin. Allowing for the unavoidable loss during the extraction and for that which is retained in the dilute alcoholic solution after separation of the crystals, the material under examination probably contains about 1 per cent. of that substance.

As far as it is at present known, santonin is not widely distributed in the genus *Artemisia*. Apart from *A. maritima*, var. a, *Stechmanniana*, Besser, the unexpanded flower-heads of which constitute commercial santonica and contain from 2 to 3 per cent., it has been found only in *A. gallica*, Willd., which is common in France.<sup>3</sup>

Arrangements are now being made for the collection of roots, leaves, and flowers of *A. brevifolia* at varying stages of development, in order to determine in which part of the plant and at what period the highest percentage of santonin is to be found. The results of the examination of this material will be reported in due course.

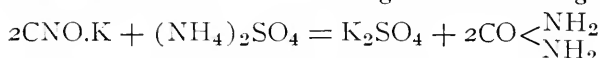
In view of the high price of santonin and the scarcity of the drug, the possibility of obtaining a supply from material growing wild and in quantity within the bounds of the empire must be regarded as a matter of importance.

<sup>3</sup> Heckel and Schlagdenhauffen, *Comptes Rendus*, Vol. 100, p. 804 (1885).

## THE DETERMINATION OF UREA BY XANTHYDROL.\*

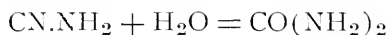
By M. FRENKEL.

In 1828 Wohler made urea according to the following reaction:



This great triumph of the materialists demonstrated urea as a product of the laboratory obtained from materials in part mineral.

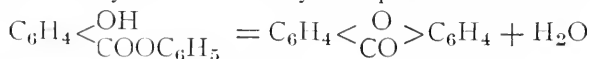
Of the different methods of preparation, the most important industrially consists in the hydrolysis of cyanamide:



The industrial uses of urea are diverse. When impure, it is added to fattening food for poultry. Pure urea is essential for the preparation of certain medicinal products such as the urethanes, veronal or diethylbarbituric acid.

A good analytical method for determining urea in a mixture with the different substances that accompany it in the course of its manufacture, is important. In the process of hydrolysis of cyanamide, the impurities obtained are ammonia, the cyanamide, the dicyanamide and dicyandianide. In the method wherein sodium hypobromite is used, not only urea but also the ammonium salts, which the urine contains as well as creatinine are determined. Therefore a precise and expeditious method for the determination of urea in urine is desired. Heretofore, all the nitrogen liberated in the hypobromite reaction has been attributed to urea. In reality, this nitrogen is due, not only to urea, but also to ammonium salts, the acid amines, creatinine, the oxyproteic acids, etc. Again, all the nitrogen of the urea is not set free by the sodium hypobromite. All the methods for determining urea in mixtures with nitrogen compounds, based on the employment of sodium hypobromite, have no value.

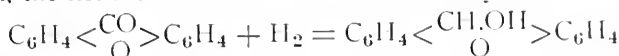
The xanthydrol method, brought forth by M. Fosse, for the determination of urea gives excellent results. If phenyl salicylate is distilled, an anhydride of o-dioxybenzophenone is formed:



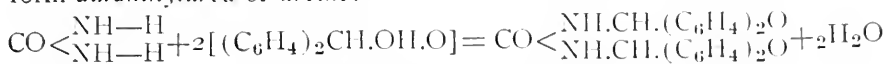
This product is also called *xanthone*. By reduction with sodium

\**Annales de Chimie Analytique et de Chimie Appliquée*, August, 1920, page 234. Abstract prepared by V. O. Homerberg.

amalgam, the xanthone is transformed into *xanthydrol*:



Xanthydrol in the presence of acid, condenses with the urea to form *dixanthylurea* or *urcine*:



$$\text{The ratio of the molecular weights} = \frac{\text{dixanthylurea}}{\text{urea}} = \frac{420}{60} = 7.$$

Xanthydrol is a white substance, light, inodorous, and insoluble in water. At ordinary temperature 1 gm. dissolves in 7 cc methyl-alcohol, and in 10 cc ethyl alcohol. Its point of fusion is about 173°.

In order to operate under the best conditions, the precipitation should be made in solutions containing about 1 to 2 gm. of urea per liter. Use 10 cc of this solution, which represents from 10 to 20 mgr. of urea. From 70 to 140 mgr. of dixanthylurea should then be weighed. The xanthydrol should be employed in a 1:10 methyl-alcoholic solution.

The determination of urea in urine is carried out in the following manner:

Take 10 cc of urine diluted to 100 cc, add 35 cc of crystallizable (glacial) acetic acid; add, while agitating, 1 cc of the reagent; continue adding, every ten minutes, 1 cc of the reagent until 5 cc have been added; set aside for one hour; collect the precipitate of dixanthylurea on a small tared filter; after draining, wash with about 20 cc of 95 per cent. alcohol added in small portions; dry at 100° and weigh. The weight, divided by 7, represents the quantity of urea.

The following substances can accompany urea in the urine without forming a precipitate with xanthydrol in the presence of acetic acid: ammonia, methyl or dimethylamine, guanidine, creatine, creatinine, arginine, glycolic acid, hippuric acid, alanine, leucine, asparagine, aspartic acid, glutamic acid, tyrosine, uric acid, xanthine, albuminoids of the egg and of the blood, fibrin, gelatin, peptone, glycerin, erythrite, mannite, glucose, levulose, saccharose, dextrin, the lactic acids, tartaric and citric acids. Such bodies as cyanamide, dicyandiamide, and dicyandiamidine are equally indifferent.

Xanthydrol can also be used for the determination of urea in the blood. To rid the serum of albumin, the following solution is used:

Mercuric chloride .....	2.71 Gm.
Potassium iodide .....	7.20 Gm.
Acetic acid, Glacial .....	66 Cc
Water .....	100 cc

Take 20 cc of serum, add 20 cc of this reagent; mix and then filter; take 20 cc of the filtrate, corresponding to 10 cc of the serum; add 20 cc of glacial acetic acid, then 2 cc of methyl-alcohol solution of xanthidrol; allow to stand one hour and then proceed as with the urine.

If solutions of urea contain mineral acids, neutralize first with ammonia, and then proceed with the filtrate previously acidulated with acetic acid.

## PREPARATION AND STANDARDIZATION OF THE EXTRACT OF NUX VOMICA.\*

By M. E. DUFILHO.

The preparation of the extract of *nux vomica* can be divided into four parts:

1. The exhaustion of the powder of *nux vomica* (mesh 22) by alcohol of 70 per cent., followed by the distillation and concentration of the tincture to the state of liquid extract, representing the fifth part by weight of the drug.

2. The cleaning of this extract by successive washes with ether, in a manner to take up all of the oily material which it contains. This oily matter will not permit the absolute drying of the extract, nor its homogeneous mixing with the sugar of milk and injures the good preservation of the product.

3. Standardization of the alkaloids.

4. Concentration to the state of a dry extract, and bringing this to the standard of 16 parts per 100 of total alkaloids, by the addition of sugar of milk.

I. Concerning the first part, the French Codex (1908 edition, page 276) gives sufficient details to permit the pharmacist to obtain a liquid extract of proper concentration. I shall criticize

\**Bulletin de la Société de Pharmacie de Bordeaux*, March, 1920, page 173. Abstract prepared by Victor O. Homerberg.



simply the fact that the quantity of alcohol employed is notoriously insufficient to exhaust completely the powdered *nux vomica*. I have already shown, in my thesis for Doctorate in Pharmacy, that in limiting the quantity of alcohol at 70 per cent. to only six times the weight of the drug, a month is necessary in order to extract all of the alkaloids of *nux vomica*, *provided that there is previously obtained each day*, by the method of macero-percolation, a weight of percolate equal to only the fifth part of the weight of the drug, the velocity  $V$  of macero-percolation being equal to  $\frac{P}{5}$ . In complying to the rules of percolation prescribed by the Codex (p. 383), experience proves that there is necessary a weight for dissolving at least equal to twice the weight of the drug.

II. *Cleaning of the Liquid Extract*.—In order to understand well the manner of this delicate operation, it is necessary to read again the directions of the *Belgian Pharmacopœia* (1906 edition, page 218). Here some of it is explained: "Extract the *nux vomica* with alcohol and concentrate to a weight of 200 gm. If the liquid does not redden litmus, acidulate it with acetic acid. Add 100 cc of ether, agitate carefully, decant the ether, repeat this washing as long as the solvent takes up oily matter. Evaporate to dryness the product thus exhausted by the ether." These few lines are clear and concise. They denote that the liquid extract of *nux vomica* contains at the same time oily matter and alkaloids (strychnine and brucine) in the state of neutral salts or readily acid to litmus. If the reaction is neutral or alkaline (which is extremely rare), that proves that there can exist in the liquid extract, free alkaloids, not salified, which will risk being carried away by successive washings of the ether. It is necessary therefore to begin by salifying, if there is need of, these alkaloids by a sufficient quantity of diluted acetic acid, after which the washing with ether can be effected without fear; the weight of the alkaloids carried away by ether should be negligible. It is advisable to place the flask containing the mixture of liquid extract and ether in a freezing bath, in order to avoid the formation of an emulsion. It is admitted to be less precise than that of the French Codex, which fixes exactly the number of ether washings, and the quantity of ether to employ for each washing. Now, that quantity is almost always insufficient; the French phar-

macist is then placed in the disagreeable alternative of either preparing a dry extract imperfectly deprived of oil, or deviating from the very narrow lines which are laid down in the French pharmacopœia. It is this latter method which it is necessary to choose, and ignore the paragraph of the Codex, where it is stated: "Evaporate with precaution, on hot water and away from all fire, the ethereal liquids; add to the oily residue 15 cc of boiling water, then diluted acetic acid, drop by drop, until an acid reaction persists. Filter through a wet filter; wash the filter with a little water, and add the filtered liquid to the product left in the flask." After the preceding explanations, it can be understood that the addition of acetic acid to the water for the washing of the oily residue is much too late; it becomes, moreover, perfectly useless, *if an attempt has previously been made to transform the alkaloids into acetates*, insoluble in the ether.

III. *Determination of Total Alkaloids*.—I shall not describe in detail the official French procedure. This procedure is long and very delicate; it requires a great visual acuteness to grasp the final change of color of the iodeosine in the presence of a hundredth normal solution of potassium hydroxide; the result obtained is not controllable; it is more often above the real per cent. of the alkaloids.

Alfred Gilkinet has pointed out in his *Treatise on Pharmaceutical Chemistry* (edition 1910, vol. II, page 743), the possibility of replacing the Belgian gravimetric determination by a volumetric determination. He uses the hundredth normal solution of potash (each cc of hundredth normal solution corresponding to .00364 Gms. of alkaloids, estimated as equal quantities of strychnine and brucine), and advises as indicator the tincture of cochineal, or better iodeosine.

This method is as defective as the French method, and for analogous reasons. It will be permissible then to replace both by the following, which is no other than the Belgian method (*Belgium Pharmacopœia*, pages 218 and 219), which I have endeavored to render practical and of an easy application, in modifying it slightly and in completing it by a volumetric determination.

Weigh into a tared watch-glass a sample of less than 3 grammes of the liquid extract perfectly cleaned with ether. Transfer the sample to a 125 cc flask with a large mouth, and ground glass stop-

per. Transfer all of the liquid extract into the flask with the aid of successive portions of distilled water, employed drop by drop; use the rounded end of a fine glass-rod to assist in the transfer. The final volume should not exceed 15 cc. Cork the flask, agitate until a homogeneous mixture is obtained; add 50 grammes of ether, 25 grammes of chloroform agitate vigorously; add 5 grammes ammonia. Agitate again for five minutes. Allow to settle for one hour. Pour the supernatant liquid onto a dry filter, collect 50 grammes in a tared Erlenmeyer flask. Distil to dryness on a water-bath. Add 10 grammes of ether to the residue and dry on the boiling water-bath and afterwards in a hot air-bath at 100° until to a constant weight. The alkaloids thus obtained are pure, brilliant and crystalline. They are weighed accurately. They represent the strychnine and the brucine contained in 2 grammes of liquid extract. This weight multiplied by 50 gives the percentage of alkaloids present in the liquid extract.

Volumetric Control of the Preceding Result. Twenty cc of  $\frac{N}{10}$   $H_2SO_4$  are added to the alkaloidal residue; about 50 cc of hot distilled water are added. The Erlenmeyer flask is placed on a water-bath for a quarter of an hour, occasionally agitating slightly. It is filtered on a wetted filter; the filter and the Erlenmeyer flask are washed with boiling distilled water; after cooling, the filtrate is made up to 200 cc. 100 cc (corresponding to 1 gramme of the liquid extract) are taken. Ten drops of tincture of litmus are added, and  $\frac{N}{10}$  KOH is added until a change of color to violet from deep blue. Let  $n$  cc of KOH be employed;  $(20-n) \times 0.0334 \times 100 =$  total alkaloids, expressed in strychnine, contained in 100 grammes of liquid extract.

The results obtained by the three methods, French, Belgian, and the volumetric that I have explained, coincide almost exactly; *the difference is only of the order of the hundredth part*; the result of the titration by the French method is always higher than the two others. That proves that volumetric method, is as it should be, only a means of control of the gravimetric method. But the behavior by change of color with litmus has this important advantage, that it can be placed in the hands of anyone, and that it permits, in five min-

utes, the control of the gravimetric result previously obtained. In addition to this, in the special case where the extract of *nux vomica* would not be perfectly freed from oil, or again if a tincture of *nux vomica* prepared directly by alcoholic percolation had to be titrated, without passing through the cleaned extract, the figure to retain would be the volumetric result obtained after filtration on a wetted filter and elimination of the enclosed oil by ether-chloroform during the extraction of the alkaloids; the indicator reagent should always be the tincture of litmus to the exclusion of all others.

The choice of the indicator reagent should not be taken with indifference. In fact, experience shows:

1. That cochineal, helianthine and muscari give figures much higher than the reality.
2. That phtaleine begins to turn only at the moment where the greater part of the alkaloids has been titrated.
3. That iodeosine, with which the change of color is clear enough, although difficult to appreciate, is practically not to be found in a pure state.

It is then to the tincture of litmus that preference has to be given. In my method, the results are expressed in pure strychnine (coefficient 334); but *nux vomica* and St. Ignatius bean contain at the same time strychnine and brucine, associated in variable proportions. The coefficient 334 that I have chosen is not then more exact, a priori, than the coefficient 364, proposed at the same time by the French Codex and by Gilkinet, as corresponding to an equal weight of strychnine and brucine. Have the authors who have busied themselves with this question exhausted the *nux vomica* and have they assured themselves that strychnine, much less soluble than brucine, requires a much greater time in order to pass completely into solution?

By prolonged macero-lixiviation, there is obtained after thirty days' treatment, an almost insipid percolate, which corresponds to a dilution of about  $\frac{1}{500,000}$ , expressed in strychnine; the exhaustion is then nearly complete. The extract of *nux vomica* prepared under these conditions, should therefore include almost the entire amount of strychnine contained in the seed. Now the gravimetric determina-

tion and the volumetric titration with litmus, agree almost exactly, if the number 334 is admitted as the coefficient, which is the molecular weight of strychnine. It appears then that nux vomica contains much more strychnine than brucine. It is the last point that I propose to determine in a further study.

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### THE CHARACTERISTIC MICROCHEMICAL TEST OF IODIC ACID WITH AMMONIA GAS.\*

M. Denigés<sup>1</sup> has shown that iodic acid can be employed to characterize, by microchemical means, the soluble or insoluble compounds of calcium, strontium and barium; this reagent does not give satisfactory results with the salts of potassium or of ammonium, but it does react with ammonia gas; if a glass slide carrying a small drop of a solution of iodic acid is exposed for a short time to the open mouth of a bottle of ammonia, the little drop will get cloudy with flat, quadratic plates of ammonium iodate, which act on polarized light and are easily recognized under the microscope. The reaction is characteristic, no volatile amine giving it.

When it is desired to apply this reaction to the investigation and to the identification of salified ammonia in a solution, a drinking water, etc., a certain quantity is evaporated until reduced to 1 cc, which is introduced, with .50 Gm. calcined magnesia into a short glass tube, 3 to 4 cm. in length and of a diameter of 15 to 25 mm., and enlarged rim, of a shape so that it is possible to maintain it upright in a sand box serving as a support. There is laid, on the middle of a slide object-holder, a minute drop of a solution of iodic acid not exceeding 2 to 3 mm. in diameter, the tube is covered with this inverted slide, the little drop facing the axis of the tube; at the end of a rather short time, the glass slide is examined under the microscope. If the liquid residue contained in the tube contains only 1 mgr. of salified ammonia, it exhibits, at the end of a few minutes, the presence of quadratic crystals of ammonium iodate corresponding to the formula  $\text{NH}_4\text{IO}_3$ .

\*Translated from *Repertoire de Pharmacie*, August, 1920, page 229. By V. O. Homerberg.

<sup>1</sup> *Comptes rendus de l'Academie des Sciences*, July, 1920.

## VANILLA PRODUCTION IN MEXICO.\*

BY TRADE COMMISSIONER CHARLES H. CUNNINGHAM.

At present Mexico employs over 50,000 people in the cultivation and extraction of vanilla—one of the most important of the minor extractive industries of that country. Vanilla is indigenous to the soil of Mexico. It is principally cultivated in the districts of Papantla and Misantla in the State of Vera Cruz, the most productive region lying southeast of Tuxpan, between the Rivers Nautla and Tuxpan.

## CONDITIONS FAVORABLE FOR GROWTH OF VANILLA PLANT—MISANTLA VARIETIES.

Vanilla grows more or less in a wild state in the low hills, and with such abundance that it perfumes the air in the vicinity. Formerly this wild vanilla was considered common property. A French colony established on the banks of the Nautla River, which engaged in the cultivation of vanilla on a large scale, met with very satisfactory results. The vanilla grows best in rich, sandy soil not drained too thoroughly. When growing wild it is usually sheltered by the trees of the forest, and in the state of cultivation it is protected by trees planted for that purpose. The temperature most favorable for its production is about 85° F. It grows best at an altitude of 1000 feet above sea level. The character of the soil, the temperature, humidity, etc., influence the quality of the vanilla, its aroma, and its strength.

There are different varieties of vanilla in the vicinity of Misantla, known as the Misantla beans, which have a coarse bark. They are not so plentiful nor are they considered so good as the Papantla bean. These indigenous varieties are the cimarrón, the mestiza, and the mansa. When they are cured only an expert can distinguish between the various classes. There is also a wild bean known as the vanilla platano, which the Indians eat. This differs from the ordinary vanilla above described (*planifolia*) in that the plant is much smaller but has larger leaves.

## HARVESTING PERIOD.

Vanilla ripens most extensively in January and February. However, there is so much demand for the fruit that for many

\* From *Commerce Reports*, Nov. 20, 1920.

years crops have been prematurely harvested in October and November. As a result the beans weigh a pound less per thousand than they would normally. In compliance with an order of the Government, the authorities were formerly instructed to prevent the harvesting of unripe fruit, but this order has not been enforced. A great deal of that which is produced early is stolen by natives, who realize that they can place the product on the market to good advantage. Many planters have their domiciles and headquarters at a considerable distance from their plantations, and in order to avoid the plundering of their crops they cut the vanilla early, rather than be deprived entirely of the fruit. One of the great problems of the owners of vanilla plantations is to provide against the robbery of their crops.

#### CLASSES OF VANILLA BEANS.

For commercial purposes vanilla is divided into four classes: The large-fine, the small-fine, la zacate, and la basura. The large-fine and small-fine are practically of the same commercial value. The former weighs from 10 to 12 ounces, and each bean is about 20 centimeters long; the latter is from 10 to 15 centimeters and its weight is almost equal to the large-fine. The zacate, which is a large vanilla bean weighing more than the former two, grows more abundantly along the roadsides in the warm and hot regions of Mexico, where formerly its fruit was considered to be without commercial value.

#### PRICE OF VANILLA—QUANTITIES AND VALUES DURING REPRESENTATIVE YEARS.

Because of the fact that the United States buys most of the vanilla of Mexico the dollar is the basis of price, both for buying and selling. The price paid at the plantation varies from about \$2.50 to \$3 per pound, while the price in Vera Cruz is about \$3.50 per pound. The New York price is about \$4.50 per pound, with duty paid. Mexico levies an export duty of 1 peso per kilo plus a surtax of 10 per cent. These have been the ruling prices for 40 years.

In 1912-13 exports of vanilla from Mexico to various countries were as follows:

Country.	Quantity. Kilos.	Value. Pesos.
Belgium .....	219	4,000
United States .....	267,089	2,977,355
France .....	20,939	320,207
Holland .....	987	11,909
Italy .....	132	2,000
Total .....	288,766	3,315,471

In 1918 the following quantities, with values, of vanilla were exported:

Country.	Quantity. Kilos.	Value. Pesos.
Spain .....	659	4,730
United States .....	44,346	500,275
Cuba .....	1	15
Total .....	45,066	505,020

During 1919 the following exports of vanilla were made to the countries listed:

Country.	Quantity. Kilos.	Value. Pesos.
Cuba .....	19	151
Spain .....	631	4,665
United States .....	193,663	2,266,826
France .....	3,087	61,598
Great Britain .....	1	12
Italy .....	1	6
Argentine Republic .....	1	6
Total .....	197,403	2,333,264

## THE WHORLED MILKWEED (*ASCLEPIAS GALIOIDES*) AS A POISONOUS PLANT.

By C. DWIGHT MARSH, A. B. CLAWSON, JAMES F. COUCH AND  
W. W. EGGLESTON.

(Abstracted from United States Department of Agriculture Bulletin No. 800, June 8, 1920.)

*Asclepias galioides* is one of the narrow-leaved milkweeds. The stems are erect, single or several, sometimes branching, "near woody" at the base, and from one to five feet high. The leaves are in whorls, narrowly linear, from two to four inches long. The flowers are in umbels. The species *galioides* is distinguished from



*A. verticellata* by possessing horizontal main roots and hairy pods while the last plant has long fibrous roots and smooth pods.

The plant has been suspected in recent years of causing the deaths of range animals. A large number of experiments upon sheep, cattle, and a horse is reported. These confirm the suspicions and demonstrate the very poisonous nature of *A. galioides*. The toxic and lethal doses were nearly identical; animals which were made sick usually died. For sheep 0.138 to 0.206 pound per hundredweight of animal was toxic and 0.138 to 0.22 pounds was lethal. Horses appear to be as susceptible as sheep; cattle are a little more resistant.

The first symptom exhibited by poisoned animals is usually the loss of control of the muscles; the animal staggers about and eventually falls. Salivation is present and sometimes, marked trembling, and in the horse profuse perspiration. When down the animal makes vigorous efforts to rise, but falls back, often with violence. After some time clonic spasms are observed and these continue at intervals with great violence. The animals are usually tremendously bloated. The animal throws itself into a position of opisthotonus which may be followed by emprosthotonus. Tetanic spasms occur later in the course of the sickness which are very characteristic; the head is drawn sharply to the breast while the legs are stiffly extended and the pupils are spasmodically dilated. The temperature rises markedly during the first stages of the intoxication and this may persist for some time. A temperature as high as 110.6° was noted in one sheep. The temperature, however, always becomes lower before death which occurs from respiratory paralysis. The symptoms may be divided into four fairly well defined stages: 1, a period of partial paralysis; 2, a short period of violent spasms; 3, a period of spasms accompanied by running movements; 4, a period when the spasms are of less intensity.

At autopsy there is an abnormal amount of gas in the digestive tract; the intestines and caecum are somewhat congested; the lungs, kidneys, thymus, and thyroid are found congested and there are often petechiae on the heart; the surface vessels of the brain are congested and clots may be found between the cerebrum and cerebellum; the blood vessels of the meninges of the spinal cord are unusually full and in some cases clots are found in the cervical and lumbar regions. The liver appears grossly normal.

The pathology of all these organs was investigated and the results are reported.

Experiments indicated that the plant is not a cumulative poison and that no tolerance is developed by repeated small doses. The leaves are the more toxic portion of the plant.

The chemical examination of the plant revealed the presence of several toxic substances which were submitted to pharmacological tests. The substance which produces the characteristic spasms of range poisoning is a non-glucosidic resin soluble in alcohol and most organic solvents but insoluble in water, acids, and alkalies. Two well-defined glucosides are present, both of which have a narcotic action. This action does not appear in the range cases because the amount of the glucosides is too small to exert a noticeable effect over the spasmodic toxin. Other constituents which were found are fats, a phytosterol, an orange-red coloring matter, resin acids, a non-toxic alkaloid, and sugars, one of which yields dextrosazone while the other appears to be maltose.

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## RESULTS ATTAINED BY THE BIOCHEMICAL METHOD IN THE INVESTIGATION OF PLANT GLUCOSIDES.\*

By E. BOURQUELOT.

In 1901, when the author first introduced the biochemical method for detecting the presence of glucosides in plant tissue, the number of known glucosides which were hydrolyzed by emulsin was limited to ten. These were salicin, amygdalin, æsculin, syringin, arbutin contaminated with methylarbutin, coniferin, gentiopicroin, salicinerein, and piccin. By means of the biochemical method the following fourteen new glucosides have been added to this group in the years indicated: aucubin, 1902; sambunigrin and prulaurasin, 1905; jasmiflorin, 1906; bakankosin and taxactin, 1907; verbenalin, aleuropein and erytaurin, 1908; true arbutin, 1910; meliatin, 1911; hepatrilobin, 1912; loroglossin, 1919; and scabiosin, 1920. Besides these, the new polysaccharide, verbascode, was incidentally found in mullein root. In many instances these glucosides were found in several different species, sometimes in families

\**Comptes rend.*, 1920, 171, 423, through *Pharm. Jour. & Pharmacist*, Dec. 4, 1920.

very distantly related from the botanical point of view. Syringin, first found in lilac, is also present in various species of privet and of jasmin. Arbutin is present in all kinds of pears, in the leaves of *Pyrola rotundifolia*, of *Grevillea robusta*, and of *Hakea laurina*. Gentiopicrin, at first known only in *Gentiana lutea*, has been found in six other species of gentian, also in *Chlora perfoliata* and in *Sweetzia*. Aucubin has been located in the genus *Garrya* and in the plantains. Prulaurasin of cherry laurel leaves occurs in the leaves *Cotoncaster microphylla*. Loroglossin has just been found in two other species of French orchids, besides in *Loroglossum hircinium*. In all, glucosides have been isolated from fifty-six species of plants. But this represents only a fraction of the number yet to be discovered. In the author's laboratory, up to the present time, 281 species of plants have been under investigation; of these 205 give indications of the presence of one or more glucosides. In fifty-six of these the glucosides have been isolated and identified. There remain, therefore, 149 for further identification. Since glucosides are shown to be present in three-fourths of the limited number of phanerogamous plants hitherto examined, as there is every reason to suppose that they are equally of general occurrence in the unexamined species, it is obvious that an immense field of research has been opened up by the method. This general distribution of glucosides which can be hydrolized by emulsin indicates that the part it plays in plant metabolism is not so unimportant as is sometimes assumed.

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## STAINLESS IODINE OINTMENT.\*

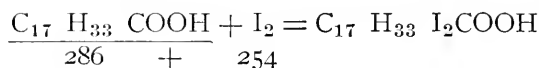
By W. P. McEWEN.

Recently there has been a call from the medical profession for a stainless iodine ointment, and to meet this demand the author worked out the following method of preparing the same, which can be readily put into practice at any dispensing counter. Ointments up to a 40 per cent. iodine content can be prepared, but the formula given here represents in strength the official ointment.

Advantage is taken of the fact that oleic acid is a member of the unsaturated series of fatty acids, and can absorb two atoms of hydrogen or their equivalent—for our purpose two atoms of iodine.

\*From *The Australasian Jour. of Pharm.*, Jan. 20, 1921.

Thus, in round atomic figures:



That is to say, 286 parts by weight of oleic acid will theoretically absorb 254 parts by weight of iodine. This would give a content of almost 50 per cent. iodine, a strength beyond medical requirements, but it shows that strengths from 1 per cent. to 30 per cent. may be readily prepared.

Four Per Cent. Stainless Iodine Ointment:—(Same strength as the official iodine ointment.)

1. Iodine, in fine powder,  $\frac{1}{2}$  oz.
2. Acid oleic, 1 oz.
3. Soft paraffin, 11 oz.

Method:—Mix 1 and 2, and warm very gently on a water bath till combination is effected, stirring well. Then add 3. Stir, and allow to cool.

As stated above, by varying the amount of iodine, and keeping the amount of oleic acid at least equal parts in weight, any strength up to 30 per cent. may be readily prepared, and if a more readily absorbent base were needed lanoline may be substituted for the soft paraffin.

### AUSTRALIAN SANDALWOOD OIL.\*

An important addition to the literature on Western Australian sandalwood oil has been published in the latest issue of the *Bulletin of the Imperial Institute* (No. 2, Vol. XVIII). Up to the present very little has been known regarding the true nature of the constituents of the oil, but viewed in the light of the official requirements for East Indian sandalwood oil, it is at once apparent that the Australian product is not suitable for medicinal use. This truth has, however, tended to obscure the purpose for which importers primarily intended the oil—namely, as a cheap substitute for Mysore oil in the soap and perfumery industries. In Western Australia practitioners, evidently, were not dismayed by the fact that the native oil failed to reach the required standard for a medicinal oil, and it has been prescribed in the Public Hospital,

\*From *The Chemist and Druggist*, Feb. 26, 1921.

Perth. Certain reports have even been made that the Western Australian oil was found to possess the properties of the true sandalwood oil without its deleterious effects. These reports were evidently considered seriously, for Western Australian authorities referred the matter to the Imperial Institute for complete tests, so that action might be taken to have the oil recognized by the British Pharmacopœia. The report now before us intimates that "the product has been investigated at the Imperial Institute with a view of determining its constituents. Experiments have also been made regarding the possibility of preparing from the Australian oil a product which would respond to the constants required by the British Pharmacopœia." Thus the investigators have had to confine themselves to the points of physical and chemical differences between the East Indian and Western Australian oils, and they wisely place the onus of recognition of the latter as a medical substitute for the Mysore product upon the therapeutic effects. It should be noted that Australian sandalwood oil is mainly derived from *Fusanus spicatus*, and the genus *Fusanus* is recognized by well-known botanical authorities so closely to resemble the genus *Santalum* that it may almost be regarded as identical and as merely a synonym, as is mentioned in the Kew Index. In testing the constants of the oil it was found that none of them, with the exception of the refractive index, falls within the range given by the B. P. for the official sandalwood product. An interesting result was obtained in fractionation experiments. The oil was distilled under 12 mm. pressure in an atmosphere of carbon dioxide, and a fraction boiling at 130°-150° C., amounting to 15 per cent. of the oil, was collected. The residual oil was again distilled, and a further fraction, boiling at 140°-150° C., under 7 mm. pressure, equivalent to an additional 15 per cent., expressed on the original oil, was removed. The effect was, curiously enough, to lower the percentage of total alcohols instead of increasing it. The explanation given is that probably the alcohol or alcohols had been partially decomposed on boiling, with the production of sesquiterpenes. An additional result of this method of distillation is that the residual oil is dextro-rotatory (unlike *Santalum album* oil, which is lævo-rotatory). A sample of East Indian oil distilled under the same conditions did not suffer similar decomposition. The next step was to subject the Western Australian sandalwood oil to steam distillation, and this method was more successful, the results showing that the

alcohols present in the oil had not suffered appreciable decomposition by distillation with steam. The oil obtained by the removal of a 20 per cent. fraction had a higher specific gravity and contained a larger percentage of total alcohols than the original oil, but these constants were not sufficiently high to met the Pharmacopœial requirements for the official oil. The report, however, states that it seems possible for an oil to be obtained by steam distillation which would conform to all the official tests except that of optical rotation. Although 20 per cent. was not, on this occasion, a sufficiently large fraction to bring about this result, on a larger scale more perfect fractionation could be obtained with steam distillation, and it should not be necessary to remove more than 20 per cent. of the oil. A similar result, it is stated, could probably be obtained by rejecting a first fraction during the original distillation of the wood. The obvious disadvantage is, of course, if no market could be found for the fraction, the loss of this quantity might render the distillation of the oil unprofitable. In determining the nature of the alcohols Chapman's oxidation method, involving the use of potassium permanganate, was followed. By this process a crystalline acid is obtained described as santalenic acid. But, while the oil from *Santalum album* yielded 24 per cent., the West Australian oil yielded only 3 per cent. Chapman obtained an average of 20 per cent. santalenic acid from East Indian sandalwood oil. This experiment gives a strong indication that the West Australian oil contains some santalol, but the smallness of the yield indicates that the proportion is much less than that of the official oil, and suggests the presence of some other alcohol or alcohols. It seems unlikely, in view of the present report, that the idea of the West Australian authorities to have the oil included in the B. P. will be realized, for conclusive evidence of therapeutic value, in so sparsely a populated country as West Australia, is not likely readily to be forthcoming. Nevertheless, the report is of value in establishing a definite relationship between the East Indian and Western Australian sandalwood oils, so that distillers, importers, and consumers may know the actual shortcomings of the cheaper oil in regard to their particular branch of industry.

# THE ALLEGED GERMICIDAL PROPERTIES OF MILK.\*

More than thirty years have elapsed since Nuttall, investigating the mechanism of natural immunity; demonstrated experimentally that blood possesses the power of killing bacteria. Soon afterward the investigation of such bactericidal power was extended to other body fluids. A somewhat comparable phenomenon has been observed in the case of milk, but the explanation of what takes place has been the subject of active debate. The facts are these: When freshly drawn milk stands without being manipulated in any way, an apparent decrease in the number of bacteria that it contains takes place within a short time. This behavior is seen only in raw milk, never being observed in milk that has been heated to any considerable extent. With respect to the temperature at which the milk is deprived of this potency, opinions have varied. A number of bacteriologists have stated that the rapid decrease in the number of micro-organisms in raw milk is apparent rather than real. They ascribe the results actually observed to an agglutination of the bacteria present so that a smaller number of colonies may exhibit themselves in the modes of counting currently employed, although no fewer organisms are actually encountered. Should this be true, it would obviously be a misnomer to speak of the germicidal properties of milk. Chambers<sup>1</sup> has recently subjected the problem to a renewed investigation at the University of Illinois. The combined evidence of microscopic examination and plate count demonstrates a bactericidal property, or actual decrease in number of bacteria in raw milk under certain conditions. Part of the earlier discrepancies lay in the failure to recognize that the germicidal action is specific, depending on the individual animal and on the species of bacteria involved. In the freshly drawn mixed milk from a herd of cows, the bacterial inhibition may therefore be variable. When only the total number of micro-organisms in the milk is considered, a decrease in numbers may be evident, or one unaffected strain by its rapid increase may completely hide the germicidal action on another less numerous strain. Chambers suggests that the predominance of lactic acid forming organisms with the increasing age of the milk might be attributed to bacterial inhibition; for these organisms are apparently unaffected by it,

\*From *Jour. Amer. Med. Assoc.*, March 12, 1921.

<sup>1</sup>Chambers, W. H.: *Bacterial Inhibition, I, Germicidal Action in Milk*, *J. Bacteriol.* 5: 527 (Nov.) 1920.

increasing immediately from the start, whereas the other organisms seem to be restrained in growth and in some cases, decreased in numbers. The germicidal property is destroyed by heating to from 80 to 90 C. (176 to 194 F.) for two minutes. Correlation between agglutinating and germicidal power has not been demonstrated. To explain the latter, one naturally thinks of a serologic origin; but this is at present nothing more than a vague hypothesis.

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## ITALIAN SUMAC PRODUCTION.\*

BY VICE CONSUL LEROY WEBBER,

PALERMO.

Sicily is the largest producer of sumac in the world, followed by the United States. The annual output in recent years is estimated at 15,000 tons, a decrease of 50 per cent., compared with pre-war production, due to the lack of cultivation brought about by war conditions. However, it is believed that it is only of a temporary nature, and with the increased demand there is expected to be a consequent increase in cultivation.

Sumac is of two kinds—male and female. The male species, which is found in the Provinces of Palermo and Girgenti, contains 28 per cent. or more of tannin, and is therefore the better of the two. The female leaf averages about 24 per cent. tannin and is generally found in the Provinces of Catania and Girgenti. Both species thrive throughout the island at any elevation up to 2000 feet.

There are about eight large sumac-grinding mills in Palermo. No works for the manufacture of sumac extract are established here, but it is believed that with the present indication of a revival of the sumac trade such works will be constructed, and plans to this effect have already been made. Exportation from Palermo is made chiefly to Great Britain, United States, France and Germany.

At present there is a slump in the sumac market, owing to the prevalent opinion that prices in the foreign markets will fall. Stocks are now available in Palermo at the following prices: Ground ventilated, 28 per cent., 73.60 lire; leaf, 28 per cent., 71.05 lire; and leaf, 30 per cent., 76.15 lire. The prices quoted are f. o. b. Palermo per hundredweight Yocum's test.

\**Commerce Reports*, 1647 (March) 1921.



## MANGANESE AS A POISON.\*

The toxicology of manganese has until recently been little understood. Used therapeutically as potassium permanganate essentially for external application, the element has not been a cause of poisoning, nor have the small quantities that occasionally find internal use in man presented toxicologic problems. Industrial workers are sometimes exposed to the dusts of ores containing considerable admixtures of manganese compounds. This is particularly true in zinc mines, where the oxids of manganese, iron and zinc occur together. Some ores also have a high content of manganese as a silicate. As the sources of menace are insoluble dusts, the chief portals of entry into the body must be the alimentary canal and the respiratory tract.<sup>1</sup> The latter is commonly borne in mind as a path of invasion when matter in particulate form is concerned. The possible effects of coal dust on the lungs of the miner and of quarry dust on those of the stone cutter are widely appreciated by those who deal with industrial menaces. Less consideration is usually given to the equally potent danger from swallowed dusts. In the case of the latter the risk depends primarily on their solubility in the alimentary secretions. Investigations of Reiman and Minot<sup>2</sup> in the Laboratory of Applied Physiology at the Harvard Medical School demonstrate that ores containing manganese as oxids and silicates are soluble in gastric juice. Manganese is absorbed in the blood stream, causing in most cases a slight temporary rise in manganese concentration followed by a quick return to normal. In none of the cases studied was the manganese content of the blood increased by the ingestion of manganese ores to a value of more than double the normal level, and in some of the subjects no increase was noted. Even prolonged feeding of large amounts of manganese ore to dogs failed to produce significant changes in manganese content of the blood and tissues or to cause any pathologic symptoms. Manganese ores are thus nontoxic, and in order to produce symptoms of poisoning

\**Jour. Amer. Med. Assoc.*, 76: 13 (March) 1921.

<sup>1</sup> Edsall, D. L.; Wilbur, E. P., and Drinker, C. K.: *J. Indust. Hyg.* 1: 183 (Aug.) 1919.

<sup>2</sup> Reiman, C. K., and Minot, A. S.: *Absorption and Elimination of Manganese Ingested as Oxides and Silicates*, *J. Biol. Chem.* 45: 133 (Dec.) 1920.

must be ingested by persons who are peculiarly susceptible. This doubtless serves to explain the comparative rarity of cases of severe intoxication caused by this element in clinical experience. Incidentally, it may be noted that manganese is far more widely distributed in traces in nature than is commonly supposed, so that it has even been rated by some as being among the essential components of living matter.

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## SCIENTIFIC AND TECHNICAL ABSTRACTS

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NATURE AND ORIGIN OF ANTIBODIES.—Sahli rejects Ehrlich's side-chain theory of the formation of antibodies, except that it is based on the sound principle that the organism is capable of responding to extra demands with extra performance, not only in the nerve and muscle systems but also in the purely chemical sphere. But Sahli does not locate the site of this extra performance in the cell protoplasm, as Ehrlich did, but in the blood and tissue fluids. The cells produce the antibodies physiologically, in response to the demands of the blood and tissue fluids, and these demands fluctuate according to conditions at the moment. The ability of a substance to act as an antigen is dependent on the property of the organism receiving it to be capable of forming the corresponding antibody, that is, it must already possess a little of the antibody, already formed. The introduction of antigen merely increases the amount formed. Diphtheria antitoxin, for example, may be found in the blood of persons and horses who have never been infected with diphtheria, and the antibodies in these and similar cases seem to be identical with the antigen-antibodies, as also with the anti-antibodies induced in other species. For instance, an antibody for sea urchin spermatozoa is found in normal rabbit serum. The absolutely infinite variety of colloidal-chemical combinations in the blood tissue fluids and lymph, explains the large number of antibodies already existent. The artificial enrichment of any antibody occurs according to the well-known laws that more is secreted to make up a deficit, and that this secretion is always carried to an excess beyond

the actual need. Antibody production is thus nothing more than one form of the physiologic regeneration of the blood, this regeneration carried to excess. The antigen and the antibody unite in a colloidal combination, and this shuts off the functioning of the antibody from the blood. The organism responds to this loss of the antibody functioning by an extra secretion to produce more of the antibody. Accepting the above three premises entails the further premise that the blood is a secretion, and he presents an array of arguments to sustain this view.—From *Schweizerische medizinische Wochenschrift*, Basel, through *Jour. Amer. Med. Assoc.*, Jan. 29, 1921.

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#### CHEMICAL CONSTITUTION AND TOXICITY TO WIREWORMS.—

The relationship between chemical constitution and toxicity to wireworms of organic compounds is found to be of a two-fold nature. The general effect of a group of compounds of the same type is directly determined by the chemical constitution of the type. The particular effects of individual members of the groups are limited by their physical properties, such as volatility, etc., which may be regarded as indirect consequences of their chemical constitutions. The aromatic hydrocarbons and halides are on the whole more toxic than the aliphatic hydrocarbons and halides. The groups which influence toxicity most when introduced into the benzene ring are, in order of importance, the methylamido (most effective), dimethylamido, hydroxy, nitro, amido, iodine, bromine, chlorine, methyl groups (least effective). But this order is modified in presence of another group; thus when there is a methyl already present in the ring the order becomes chloride (side chain), amido, hydroxy, chlorine (ring) methyl. Chlorine and hydroxy groups together give rise to highly poisonous substances considerably more effective than where present separately. The association of chlorine and nitro groups in chloropicrin gives rise to one of the most toxic substances tested. Methyl groups substituted in the amido group of aniline increase toxicity more than if substituted in the ring. Compounds with irritating vapors usually have high toxic values. In a series of similar compounds decreases in vapor pressure and in volatility are associated with an increased toxicity. A limit is put on toxicity by the decrease of vapor pressure when it sinks

too low to allow a toxic concentration in the vapor phase. Nearly all compounds boil above  $215^{\circ}$  C. are uncertain in action and those which boil above  $245^{\circ}$  C. are non-toxic. (Tattersfield and Roberts, *J. Agric. Sci.* 10, 199-232 [1920].)

J. F. C.

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GERMICIDAL VALUE OF CHLORINE DISINFECTANTS.—Dr. F. W. Tilley, of the Biochemic Division, Bureau of Animal Industry, has recently published the results of a very careful investigation into the germicidal value of chloramin T, Dakin's solution, eusol and chlorine. He concludes: In the ordinary routine of general disinfection, such as disinfection of cattle pens and cars, there is always a large amount of organic matter present. It is evident, therefore, that because of the enormous diminution in germicidal value on addition of organic matter as well as because of the injurious effects on metals and fabrics the chlorine disinfectants as a class do not seem to be suited for use under the usual conditions and by the usual methods of general disinfection. That is not to say, however, that when properly used they are not efficient and valuable in the treatment of infected wounds; in fact, the evidence available goes to show that they are of great value when so used; and, of course, chlorine and hypochlorites are very widely and successfully used for the disinfection of drinking water. Compared on a basis of weight of Chloramin T as against weight of chlorine as sodium hypochlorite (Dakin's solution) or hypochlorous acid (eusol), or as chlorine in aqueous solution, Chloramin T is less efficient than the others. But if the comparison is made on the basis of available chlorine contained it is much more efficient against *Staphylococcus aureus*, much less efficient against *Bacillus pyocyaneus*, and approximately equal in efficiency against *B. typhosus*. The experiments upon *Bacillus tuberculosis* indicate that the chlorine disinfectants are worth very little so far as that organism is concerned. A selective action on the part of the various disinfectants was apparent. The action of the chlorine disinfectants upon anthrax spores show that the germicidal action is not always so speedy as is commonly supposed, but may extend over several days. The addition of ammonia to solutions of chlorine or hypochlorites very greatly increases their activity. (*J. Agric. Res.* 20, 85-119 [1920].)

J. F. C.

MUSCARINE: AN INTERESTING ALKALOID.—Muscarine, although non-official and virulently toxic, is nevertheless an alkaloid of no little interest physiologically. As the active principle of the fungus *Agaricus muscarius*, it has often caused fatalities by being mistaken for the edible fungus *Agaricus campestris*. Again, Brieger has shown that muscarine is not an uncommon product of albuminous decomposition during putrefaction. It can therefore be classed as a ptomaine. Lauder Brunton many years ago suggested that the symptoms of muscarine poisoning were closely allied to those of Asiatic cholera, from which he concluded that the antidote to muscarine—atropine—would prove useful in that disease. Having excluded mushroom poisoning in cases in which the symptoms were of a choleric character, he gave doses either of belladonna by the mouth or atropine hypodermically. So directly successful were the results that the use of atropine as a cardiac and respiratory stimulant in cholera appealed to him as an encouraging method of treatment. The inference to be drawn from Brunton's observations is that muscarine as a ptomaine differs in some respects from the alkaloid derived from the fungus. (*Med. Press and Circular*, Nov. 24, 1920, through *The Pharm. Jour. and Pharmacist*, Jan. 29, 1921.)

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REACTION OF BENZOIC ACID AND ITS APPLICATION TO THE DETECTION OF ATROPINE, COCAINE, AND STOVAINE. M. Guerbet. (*J. Pharm. Chem.*, 1920, 22, 321-323.)—The reaction described depends on the conversion of the benzoic acid into a mixture of nitrobenzoic acids, reduction of these to aminobenzoic acids which are then diazotised, and the resulting diazonium compounds condensed with *B*-naphthol. The mixture of *o*-, *m*-, and *p*-naphthol azobenzoic acids formed has an orange-red color. The test may be used for the detection of atropine, cocaine, and stovaine, or other substances containing a benzoyl group in their molecule. The details of the test are as follows: About 10 mgrms. of benzoic acid are mixed on a watch-glass with 5 drops of fuming nitric acid, and evaporated on a water-bath; the residue is treated with 1 drop of 10 per cent. stannous chloride solution, heated for three minutes, cooled, and 2 drops of 1 per cent. sodium nitrite solution are added. After a few minutes, 4 drops of a 1 per cent. *B*-naphthol solution in 10 per cent. ammonia are added, when a red orange-colored pre-

cipitate is formed. If this final mixture is evaporated to dryness, the residue dissolved in concentrated sulphuric acid giving a red-violet solution which changes to yellow when the solution is poured into water. (From *The Analyst*, Jan., 1921.)

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MANGANESE IN FOXGLOVE LEAVES.—Burmahn has asserted that manganese is a constant constituent in *Digitalis purpurea*, but is not present in *D. ambigua* or *D. lutea*. Webster has now examined a number of species of digitalis, including the three mentioned above, and has found manganese in all of them. In the leaves of *D. purpurea*, the proportion present varies from 0.94 to 0.12 Mgms. in 100 Gms. of dried leaves. (*Ber. d. Deutsch. Pharm. Ges.*, 30, p. 376, through *The Pharm. Jour. & Pharmacist*, Dec. 18, 1920.)

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CHELERYTHRINE.—Bauer and Hedinger have prepared chelerythrine from *Sanquinaria* rhizomes by mixing the drug with milk of lime, drying on a water bath, and extracting the alkaloids with a mixture of equal parts of ether and benzine. From this solution they were removed by solution of citric acid, and, after the addition of ammonia, transferred to benzene. On evaporation of the benzene solution the total alkaloids are obtained. The proportion found varied from 0.66 to 1.74 per cent. From this mixture chelerythrine can be obtained by repeated crystallization from alcohol. It is readily soluble in chloroform and benzene, less readily in alcohol, ether, acetone, and methyl alcohol. The chloride crystallizes in yellow needles of the formula  $C_{21}H_{17}NO_4H_2O$ , the iodide in dark red needles; oxalate, reddish-yellow. The presence of a methoxy group could not be detected. (From *Archiv d. Pharm.*, vol. 258, p. 167, through *Pharm. Jour. & Pharmacist*, Dec. 11, 1920.)

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PRESENCE OF HYDROCYANIC ACID IN LINSEED CAKES: E. Kohn-Abrest (*Ann. Falsif.*, 1920, 13, 482-487).—The cyanogenetic glucoside occurring in linseed is concentrated in the pressed cake obtained when the oil is expressed, but the quantity in the cake appears to depend to some extent on the method of manufacture. Much of

the hydrocyanic acid is lost during prolonged maceration of the seeds and by evaporation. Linseed grains of various origin (Indian, S. American, Russian, French, etc.), yielded about 0.02 per cent. of hydrocyanic acid; linseed cakes yielded up to 0.38 per cent. It is suggested that a maximum limit of 0.02 per cent. of hydrocyanic acid should be fixed for linseed cakes used for feeding animals. (Through *The Analyst*, February, 1921.)

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PRESERVING THE GREEN OF PLANTS.—A discovery of very great interest to botanists and others has recently been made. As is well known, when plants have been dried by any of the well-known processes (such as under pressure, in hot sand, or by sulphur fumes), the foliage loses most of its natural greenness. To get anything resembling a life-like effect, the leaves have had to be artificially colored, and this plan has not proved to be very satisfactory. The difficulty has been entirely surmounted owing to the fact that it has been found possible to form a chemical compound with the chlorophyll which is permanent.

The method adopted is on the following lines: A boiling solution of copper acetate and acetic acid is prepared. Into this, parts of the plant to be preserved are steeped. The acetate combines with the chlorophyll and forms a permanent coloring matter. Whatever the original shade of green may be, this color is perfectly fixed. The drying process can then be carried forward. Where the particular method is that which preserves the form, as in the case where hot sand is used, the plant preserved is wonderfully life-like.

The steeping in the copper acetate appears to have no effect on the flowers. If the drying is carried out with sand or sulphur fumes the original hues are usually well preserved.

The plan described has also been employed in the preservation of seaweeds with excellent results. For the brown seaweeds it has been found needful to add a little permanganate of potash to secure the best effect. With red seaweed certain stains are used, but once the right color is secured, the copper acetate fixes it for all time. One great value of this plan is that the plants so treated do not suffer from exposure to light. After some months of standing in direct sunlight the treated specimens were as bright green as if they had been freshly picked. (*American Druggist*, February, 1921.)

## MEDICAL AND PHARMACEUTICAL NOTES

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ADULTERATION OF GUM TRAGACANTH WITH GUM ARABIC: L. Thevenon. (*Ann. Falsif.*, 1920, 13, 489.)—Powdered gum tragacanth is sometimes adulterated with the cheaper gum arabic. The presence of the latter may be detected by treating a portion of the sample mixed with water with an equal volume of 4 per cent. pyramidon (dimethylaminophenyldimethylpyrazolone) solution, and then adding 10 drops of hydrogen peroxide (12 vol.). A blue-violet coloration develops within five to thirty minutes, according to the quantity of gum arabic present. The test will detect as little as 1 part of gum arabic in 20 parts of gum tragacanth. (Through *The Analyst*, February, 1921.)

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RESERVES OF VITAMINS IN THE ORGANISM.—Lumière presents arguments against the assumption of reserves of vitamins, and in favor of his view that the vitamins act by stimulating the digestive glands. When deprived of vitamins, the digestive glands cease to function more or less completely. They may continue to function for a little time—which has erroneously led to assumption of reserves of vitamins. The prompt recuperation when vitamins are resupplied after the deficiency disease has developed, is further testimony of their stimulating action on the digestive glands as the latter start at once to function anew. No other explanation fits with the promptness of this recuperation. One of his arguments refers to the special task of the cerebellum in birds as controlling orientation in flight. This special development of the cerebellum requires an extra amount of nourishment for it. When the nourishment is shut off by lack of vitamins, the cerebellum suffers first and foremost from this lack of nourishment, so that the cerebellar symptoms are the first and predominant ones to appear. (*Paris Médical*, December 18, 1920, through *Jour. Amer. Med. Assoc.*, February 19, 1921.)

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THE STERILIZATION OF INSTRUMENTS.—Rebula states that in many text books on surgery instructions for the sterilization of instruments read somewhat as follows: "Instruments may be sterilized by boiling in a 1 per cent. soda solution, which also prevents



rusting." That such inaccurate statements should be made by famous surgical experts he finds quite pardonable, since "*de minimis non curat prator*," but does not think that such nonsense should be perpetuated in the smaller text books destined for the use of nurses. He asserts that neither sodium carbonate nor sodium bicarbonate will prevent the rusting of instruments. It is the carbon dioxide in the water that causes the instruments to rust. Neither sodium carbonate nor sodium bicarbonate combines with the carbonic acid of the water. In order to prevent the rusting of instruments 2.5 gm. of sodium hydroxide (NaOH) should be added to 1000 gm. of water. The sodium hydroxide should be allowed two minutes in which to dissolve and to combine with the carbonic acid of the water, before the instruments are put in the solution. (*Zentralblatt für Chirurgie, Leipzig*, through *Journ. Amer. Med. Assoc.*, February 19, 1921.)

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BENZYL BENZOATE IN PEDIATRIC PRACTICE.—Ruhräh states that benzyl benzoate may be used in place of atropine wherever a relaxing effect is desired on spasm of smooth muscle. He recommends it in bronchial asthma, spasmodic bronchitis, gastric or intestinal colic, hiccough and spasmodic constipation. In whooping-cough, he says, its action is often most beneficial, but the results are uncertain, as is the case with all other antispasmodics in this disease. In general convulsive conditions not dependent on organic lesions of the central nervous system, especially in the new-born, the drug is of benefit. (From *Amer. Jour. of Med. Sciences, Phila.*, through *Jour. Amer. Med. Assoc.*, Feb. 12, 1921.)

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PICRIC ACID IN OPERATIVE SURGERY.—Picric acid, Farr says, is ideal as a skin application preceding operation in that it never irritates and that it remains in the skin for a long period of time. Its only drawback is its rather startling color, which may annoy sensitive patients when exposed surfaces are stained. From the clinical standpoint, Farr's results compare very favorably with those formerly obtained with iodine and with the older methods of skin preparation. (From *Annals of Surgery, Phila.*, through *Jour. Amer. Med. Assoc.*, Feb. 12, 1921.)

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ACRIFLAVINE TREATMENT OF GONORRHEA.—The technic employed by Mann is that of Watson, who uses a 1 : 4000 solution of acriflavine in physiologic sodium chloride solution, at body tem-

perature, once daily. He regards this as being the best remedy for the irrigation treatment of gonorrhea and analyzes thirty-six cases, carefully controlled, in which he made use of the treatment. (From *Medical Record, New York*, through *Jour. Amer. Med. Assoc.*, Feb. 12, 1921.)

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THE WASSERMAN REACTION OUTSIDE OF SYPHILIS.—Touraine records a number of tropical diseases which give a positive Wassermann. Leprosy gives the reaction in 47 per cent. of cases. Pulmonary tuberculosis is known to have reacted in 197 out of 848 cases, lupus in 50 per cent. of cases. Even a prolonged ether or chloroform narcosis will give a positive Wassermann in about 25 per cent. of instances. A number of blood diseases (hemoglobinuria, leukemia) occasionally also contribute to the source of possible errors. Author warns against a one-sided conclusion in the basis of positive Wassermann. (From *Revue de Médecine, Paris*—37, No. 2, 1920, through *Jour. Amer. Med. Assoc.*, Dec. 18, 1920.)

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## NEWS ITEMS AND PERSONAL NOTES

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DECEASE OF PROFESSOR ELIE BOURQUELOT OF FRANCE.—The death is announced in Paris of Professor Elie Emile Bourquelot, Chevalier of the Legion of Honor, Vice-President of the Academy of Science and the Academy of Medicine. Professor Bourquelot was born in Jandun in 1851. He passed his examination for the degree of *docteur ès sciences* in 1884 and became professor of pharmacy in the Paris School of Pharmacy in 1897. From 1886 onwards the name of Professor Bourquelot is of frequent occurrence in the index of the "Year-Book of Pharmacy," as the author of pharmacological monographs. In 1909 he was present at the International Congress of Applied Chemistry in London, and contributed a paper on "The Employment of Emulsin in Testing for Glucosides in Vegetable Products." At the International Congress of Pharmacy at The Hague in 1913 he read a monograph on "The Synthesis of Glucosides by Ferments." His well-known book on soluble ferments was published in 1896. As editor of the *Journal de Pharmacie et de Chimie* and as a brilliant man of science his reputation was world-wide. An abstract of a paper prepared by Professor Bourquelot appears in this issue of the JOURNAL.

DECEASE OF H. B. ROSENGARTEN, PHILADELPHIA.—Harry B. Rosengarten, President of the Powers-Weightman-Rosengarten Company, died at his home in Philadelphia on February 19th, after a brief illness. Mr. Rosengarten, who was eight-four years of age, was stricken with paralysis on his birthday, February 16th.

He was born in Philadelphia and educated in the private schools of that city. He then entered the business of his father, the founder of Rosengarten & Son, which was consolidated with the firm of Powers & Weightman into the present Powers-Weightman-Rosengarten Company.

Mr. Rosengarten was connected with the great chemical house for more than sixty years and during that long period gave his steady attention to the affairs of the company. During that time he not only earned the respect and admiration of his friends in business but was also very popular with the employees of the offices and plants.

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W. C. VAN BERGEN WITH NORWICH.—The Norwich Pharmaceutical Company, of Norwich, New York, announce the appointment of W. C. Van Bergen as advertising manager, vice Geo. L. Vander Veer, deceased. Mr. Van Bergen's broad advertising and merchandising experience will doubtless prove of value in furthering the policies of the House of Norwich.

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PHYSICIAN-GRADUATES OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.—When a college reaches its century mark it begins to take a correcter account of those who have graduated from its courses, and it frequently finds data which is quite surprising. We have had recourse recently to a list of living graduates of this institution who have become practicing physicians. We find colonels in the Army, a surgeon-general of the navy, rear-admirals, presidents of State societies, prominent specialists in the various branches of medicines, professors, instructors, hospital superintendents, medico-legal experts, etc., an array well worthy of the College that gave them their diploma in Pharmacy. Nearly five hundred graduates of the College constitute this list referred to.

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THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE OUTLINES A PROGRAM OF PROGRESS AND SERVICE.—The Philadelphia College of Pharmacy and Science, the oldest institution in

America for the training of druggists and pharmacists, is celebrating its century of growth by inaugurating a definite series of changes and advancements, almost as epoch-making as was the founding of the institution in Carpenters' Hall, Philadelphia, in 1821.

The project includes an endowment fund, new officers, new buildings, a new site and a new programme of service to the science of Pharmacy and to humanity.

The first step to bring about the new order of things was taken on March 28, when, at the most largely attended meeting the college has held in a quarter of a century, Otto W. Osterlund was elected president of the college in the place of Howard B. French, Frank R. Rohrman was chosen to succeed Richard V. Mattison as first vice-president, and Ambrose Hunsberger to succeed Charles A. Weidemann as recording secretary. Ivor Griffith was named as the editor of the *AMERICAN JOURNAL OF PHARMACY* in the place of George M. Beringer, who resigned.

Mr. Osterlund assumes his new duties at the height of a successful business career. He was born May 28, 1874, and was graduated from the Philadelphia College of Pharmacy with the class of 1899, of which he was vice-president. He is a former president of the Alumni Association of the College and of the Philadelphia Association of Retail Druggists. Formerly he maintained two flourishing drug stores in Philadelphia, but left this business recently to assume the presidency of the Belmont Trust Company. He is a treasurer of the Pennsylvania Board of Pharmacy, having been appointed to the board successively by Governors Tener, Brumbaugh and Sproul.

Frank R. Rohrman, the new vice-president, is president of the Philadelphia Wholesale Drug Company. Ambrose Hunsberger, the new secretary, is a retail pharmacist. Ivor Griffith, the new editor of the *AMERICAN JOURNAL OF PHARMACY*, is instructor in Pharmacy and Pharmaceutical Arithmetic at the Philadelphia College of Pharmacy and Science. It is understood that Mr. Osterlund is taking the presidency only until such time as a man of national reputation who can devote his entire time to the college can be procured. On assuming his new duties, Mr. Osterlund said:

"I believe that an institution of the high character and importance of the Philadelphia College of Pharmacy and Science needs a man of unusual attainments at its head. He should be a scholar—a man of wide reputation. He should possess a magnetic per-

sonality and the faculty of winning friends for the institution. And he should be enabled to devote all his time and energy to the upbuilding of the college. With the trustees and members I shall seek diligently for such a man to take the place I am now filling temporarily.

"In the meantime, there is every assurance of success for the college, not only in the immediate task of raising funds to develop the institution and broaden the scope of its work, but in the task of increasing its usefulness to humanity. I know we will have one hundred per cent. co-operation from the retail druggists of Philadelphia, and I believe the druggists generally throughout the country will support us whole-heartedly."

The first task of the new administration will be the raising of a two-million-dollar endowment fund. For a century the college has derived nearly its entire income from tuition fees from students and dues from members and the work has necessarily been hampered. Notwithstanding this fact, the Philadelphia College of Pharmacy and Science has maintained the lead it took in 1821, and has made many valuable contributions to the sciences of Pharmacy and Materia Medica. As an example of the recognition accorded it, one might mention the Revision Committee of the Pharmacopœia, where not only is the chairman, E. Fullerton Cook, a Philadelphia College of Pharmacy professor, but twelve out of the thirty-three pharmacists on the committee are alumni of the institution.

Because of the remarkable contributions to science and to the profession of Pharmacy made by the college, the officers and trustees have every confidence in a generous response on the part of the public. With the fund to be raised scholarships will be endowed, a new site in the most highly desirable section of Philadelphia will be obtained, administration and research buildings will be constructed and the foundation laid for growth and progress in keeping with the history of the college.

Already an option has been secured on a large plot of ground facing the new Fairmount Parkway, which is being developed as one of the most beautiful thoroughfares in the United States. An architect is drawing plans which call for a central administration building with four wings to house research laboratories.

To raise the endowment fund desired, the entire country has been divided into districts, in each of which a committee has been elected by graduates of the institution residing in that particular

territory. Inasmuch as there are more than five thousand living alumni in the United States, to say nothing of those in foreign lands, the Philadelphia College of Pharmacy and Science is confident of success in carrying out its new programme for growth and service.

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## BOOK REVIEWS

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"GENERAL AND INDUSTRIAL CHEMISTRY, ORGANIC." Part I, Second Edition. By DR. ETTORE MOLINARI, translated from the Third Italian Edition by Thos. H. Pope, B. Sc. \$8.00 net. P. Blakiston's Son & Co., Philadelphia, Pa.

This work, containing 254 illustrations, covers in 441 pages what appeared in 369 pages of the first English Edition, but the gain is more apparent than real, as the type used in the fine print articles, of which there are a large number, is between 15 and 16 per cent. larger than that used in the previous edition. This accounts in large measure for the increased number of pages devoted to such industries as those of Illuminating Gas, Petroleum, and Ethyl Alcohol.

There is considerable new matter, however; for instance, a half-page on Alcohol from the Sulphite Liquors from the Paper Works, two-thirds page on Alcohol from Calcium Carbide, a half-page on the Recovery of Ether from the Air, a half-page on Chemistry and the War, and, here and there, smaller items of new matter.

A number of articles have been rewritten, notable among these being those on The Industrial Preparation of Methyl Alcohol, and Tests for Methyl Alcohol. Nearly all, probably all, of the matter has been reset, much of it without change of language; with the result that the book contains some statements which were true when the first edition was written but not now, and others which were doubtful as to truth when first written are perpetuated in the new book. For example, on page 34 (33 in 1st Ed.) we read "at Pittsburg there are great wells of pure methane," doubtless referring to the very prolific natural gas wells which, for a number of years about the beginning of the present century, made that city undeserving of its title "The Smoky City," but which for a dozen or more years past have been little more than a pleasant memory. On page 119 we read "the use of chloroform has been suggested to render

pigs insensible, so as to kill them painlessly and to skin them more easily. Also, in fattening them, they are subjected to periodic inhalations of chloroform, which renders them more restful." In the first edition this read "In America chloroform is used to render pigs insensible," etc. It is very gratifying to feel that the Italian author and his English translator had such a fine idea of the, shall we say, "humanitarian" or "swinecaterian" instincts of Americans, but we doubt that any visitor to any one of the great abattoirs of the Middle West, or to any pigsty of the East or West, could detect anything chloroformic in the odors that greeted his nostrils.

As in the first edition, there is a wealth of statistical matter, some of it up-to-date, but much of it admittedly not so, World War conditions making it impossible to secure accurate statistical data. It has some value, however, and the book would be the poorer without it.

Frequent reference is made to matter found in the author's work on Inorganic Chemistry under the designation "Volume I." This offered no difficulty while the subject of Organic Chemistry was confined to one volume, but we can see where some confusion might result if the same style of reference were to be continued in the second volume of the two-volume edition.

The book is one which we can unhesitatingly recommend, both as a text-book and a reference book, presenting, as it does, in a clear and very readable form, both the theoretical and practical aspects of the chemistry of a large number of important classes of aliphatic compounds. We await anxiously the appearance of the second volume.

F. P. STROUP.

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"SYNOPSIS OF PHARMACOLOGY." By DOUGLAS COW, M. D., Examiner in Pharmacology, University of Cambridge. Published by L. & A. Churchill, London, 1920.

According to the statement of the author, this book is not intended to replace "recognized text-books," but to be used rather as a review manual by students.

The titles are arranged in alphabetical order, thus avoiding the need of an index. The cross indexing introduced in this arrangement is quite valuable. Information is very concisely given, and, considering the scope of the work, is remarkably complete.

The illustrations and the legends accompanying them are of

such a character and so arranged as to constitute very easily understood charts of the activities of the various drugs.

The author shows a very thorough knowledge of his subject. Also, he appears to have a keen appreciation of the student's needs and of the student's viewpoint. This is a commendable combination which is all too rare among teachers of technical subjects.

G. M. B., JR.

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"THE MICROANALYSIS OF POWDERED VEGETABLE DRUGS." By ALBERT SCHNEIDER, M. D., Ph. D., Professor of Pharmacognosy in The College of Pharmacy, University of Nebraska. Second edition, Vol. XII; 548 pages and 237 illustrations. Price, \$5.00. P. Blakiston's Son & Co., Philadelphia.

This recent publication from the pen of Dr. Schneider represents a marked improvement over the first edition, which appeared in 1902 under the title of "Powdered Vegetable Drugs." Two hundred and twenty-five pages have been added to the subject-matter appearing in the first edition; some of the old figures have been replaced by newer ones and a number of new illustrations have been added. The contents are included in eleven chapters, which are as follows: The Microscope in Modern Pharmacy, General Suggestions on the Examination of Vegetable Powders, Quality and Purity of Vegetable Drugs from the Standpoint of the Pure Drugs Act, Causes Modifying the Characteristics of Vegetable Powders, Powdering Vegetable Drugs, Adulteration or Sophistication of Vegetable Drugs, The Microscopical Examination of Powdered Vegetable Drugs, Keys to the Study and Identification of Simple Powdered Vegetable Drugs, Keys to the Study and Identification of the U. S. P. and N. F. Compound Powders, Microanalytical Study of Crystals, Quantitative Microscopic Determinations.

The plan of the work is excellent and permits much freedom of initiative to teachers, a quality often wanting in many of our recent scientific texts. There is sufficient information within its covers to meet the requirements of a two-semester course in Powdered Vegetable Drugs. One of the particular outstanding advantages is the large number of illustrations which should be very helpful to all who use it. The analytical keys are workable and should be welcomed alike by drug and food analysts. As a reference book on Powdered Vegetable Drugs it eclipses in data any so far written by an American author.

HEBER. W. YOUNGKEN.



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## EDITORIAL

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### DYESTUFFS AND PHARMACY.

The relation existing between dyestuffs and pharmacy may not be any more apparent to our legislators at Washington than the relation between dyestuffs and explosives, or dyestuffs and chemistry, but it is a real one, nevertheless. Our State and National pharmaceutical organizations, which are planning to hold meetings during the next few months, should take cognizance thereof and pass suitable resolutions insisting upon a proper protection of this key industry up-building and maintenance of which is so vital to our peace-time prosperity and our war-time success.

We must not permit a warped and limited vision on the part of a few to bring about a condition that will do injustice to the many.

The processes by which many of our officially recognized and widely used synthetic remedies are manufactured need not be actually carried on in dyestuff plants, but the interdependence in the matter of raw materials and intermediates makes it impossible to succeed in either one of these lines of work without the other as an adjunct.

Acetanilid, antipyrin, arsphenamine, cinchophen, phenacetin, phenol, cresol and many other medicaments and antiseptics, as well as some actual dyestuffs themselves, such as methylene blue, flavine and scarlet red, are dispensed by pharmacists on the prescriptions of physicians for the prevention or cure of disease.

The maintenance of a domestic supply of these drugs, however, is of minor importance, as is also the matter of cost. What is needed is the encouragement of an industry which is helpful to research and to higher scientific education as well as in the produc-

tion of material things. The dyestuffs manufacturing industry needs protection and it needs it promptly if it is to be saved.

It is a matter of record that the only opposition to it is based on selfish motives. It is a matter of regret that the failure of Congress to act decisively and constructively in the matter, as has already been done by the Parliament of England and the Chamber in France to protect their respective countries from unfair and industry destroying competition of German manufacturers, has not been bitterly resented by every pharmacist and chemist in the land. Inertia in this respect is the cause of our present dilemma.

What we need is the kind of action that will bring to our misrepresentatives who are blocking this action, a realization of their responsibilities and to our Senators an appreciation of the fact that they may become metamorphosed into ex-Senators if they continue to obstruct scientific progress and imperil national safety.

In chemistry some reactions proceed slowly until a catalyst is added, when the speed of the reaction is infinitely increased. The catalyst needed in the reversible reaction which is now exhibiting itself in a condition of static equilibrium in our Washington legislative halls, is an active interest in every scientific body in the country. This interest would be manifested in two ways. First, by the passage of suitable resolutions on the part of the organizations themselves, and second, by active protests on the part of individual members of these organizations, voiced to their local representatives and senators in no uncertain language.

We must prevent a recurrence of the conditions from which we suffered during 1915, when prices went skyrocketing and patients suffered, and in some cases doubtless died, for lack of certain medicaments. Pharmacy can and should do its part in this important work and now is the time when help will most count.

C. H. LAWALL.

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### A GREAT PHARMACIST PASSES AWAY.

Henry P. Hynson, the American pharmacist, whose death has been announced in the journals of the profession, leaves behind him an enviable record of usefulness and attainments. His had been a life of devotion dedicated to the advancement of his profession and to the practicalizing of worth-while ideals.

His unusual personality and accomplishments made him a conspicuous figure in any assembly, but never did he indulge in meretricious artifice to attract popular applause, and disingenuous maneuvering was never perceptible in his character. He did all things with sincerity.

Possessed of an endearing personality, brusque, but versed in courtesy, he made and maintained a wide circle of friends who will inevitably miss his happy companionship and his keen humanness. A pioneer in many fields of pharmaceutic endeavor, he was largely responsible for the formulation of many organizations which now hold potent sway in pharmacy. He was the first President of the National Association of Retail Druggists, and while he differed with some of the later policies of that body, he nevertheless maintained a kind and active interest in all of its activities. In the American Pharmaceutical Association meetings he was always an outstanding figure, and did much constructive work in the development of that organization. The Section on Practical Pharmacy and Dispensing was of his conception, and it was with pride and satisfaction that he annually exhorted the incoming chairman of that section to mind well and zealously its destinies.

His particular pride, however, was in his store in Baltimore, where he reared through constant and sincere efforts a business which today is a beacon light of ethical pharmacy that sheds its message of faith and accomplishment to all the profession.

*The Journal of the American Medical Association* in commenting upon Henry P. Hynson's death and particularly upon the high standards obtaining in his establishment, thus honors his ideals in no uncertain language:

"As already suggested, his constant effort was to emphasize as of primary importance the service which the educated scientific pharmacist was in a position to render to the public, and to decry the commercial ideas which seemed to be strangling the professional instincts of the pharmacists. He opposed commercial drug store exploitation of the public with 'patent medicines' and making pharmacy a mere adjunct to the sale of soda water, light lunches and novelties. Hynson was one of the few prominent pharmacists who were willing to forego financial gain in order to raise the ethical standards of a profession which he honored. He took an earnest interest in all the live pharmaceutical questions of the day, and pure pharmacy sustained a great loss in his death."

The passing away of this great man undoubtedly leaves a void that can be scarcely filled and the sterling example of him amply blazes the trail for those who are eager to follow in the prints of his climbing foot-steps.

I. G.

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## ORIGINAL PAPERS

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### PELARGONIUM-OIL.

PROFESSOR RICHARD KNUTH,  
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The rose-oil which plays a prominent part in the manufacture of the best perfumes and is used pure as perfume and as an ingredient in the manufacture of soap, is produced not only from the petals of *Rosa damascena* Mill, but often from other plants, which have a similar odor. Such substitutes of the best sort are the pelargonium-, the palmarosa- and the gingergrass-oil. The latter two, according to Stapf (*Kew Bull.*, 1906, p. 297), are respectively termed *Andropogon schoenanthus* Flück. et Hanb., non L. and *Schoenanthus* var. *Martini* Hook f. This plant, which is widely distributed in India, is used, according to his reports, as an oil-plant in Kandesh of the Presidency of Bombay, in the districts of Nagpur, Sagar, Qabalpur, and Karnul, and in Ajmere of Radschputana. According to one opinion, the two oils are produced by different stages of development, according to another by different varieties of the same species.

The most valuable substitute for rose-oil is undoubtedly the pelargonium-oil, which is obtained from the rose-geranium. The name of this geranium dates from the time when the two genera geranium and pelargonium had not yet been separated. Linné classed most of the geraniaceæ as geranium; l'Héritier was the first to separate, in 1787-1788, the species pelargonium and erodium from geranium.

#### CLASSIFICATION OF THE PLANT.

Gintl (p. 268) pointed out in 1879 that the French rose-oil is manufactured from *Pelargonium radula*, that of Algeria from *P. roseum* and *P. odoratissimum*. The French oil is said to polarize light to the right, the Algerian, to the left. According to Heuzé (p.



1. ROSE-CERANIUM



2. PELARGONIUM ODORATISSIMUM (L.)  
AIT.



3. PELARGONIUM GRAVEO-  
LENS AIT.



4. PELARGONIUM FRAGRANS



305), the species chiefly cultivated in Algeria are *P. capitatum*, which was introduced into England from the Cape, in 1690, and, to a smaller degree, *P. odoratissimum* and *P. fragans*, which also produce a good oil, but whose cultivation is not profitable, owing to the small size of the leaves. Holmes (p. 239) says that several species of the genus are cultivated. According to Cordemoy (p. 170), only *P. capitatum* is grown on the Isle of Réunion. Likewise Charabot and Gatin (p. 289) report that the plant is generally named *P. capitatum*, but add that it was determined in the Museum of Paris as *P. graveolens* Ait. = *terebinthaceum* Cav. The two authors admit that perhaps several species come into consideration.

As a matter of fact, the classification offers great difficulties. The name *P. capitatum* is certainly false, because the species is totally different, in the form of its leaves, from the rose-geranium, which is cultivated in Algeria and on the Isle of Réunion. The plant must doubtless be placed in the group of *P. graveolens* l'Hér. It is true, plants of different localities show differences, which are not insignificant. They may be considered either as varieties of cultivation, or as hybrids of other species, whose origin is now unknown or has been forgotten long since. To understand this, it may be remembered that in the beginning of the nineteenth century there was a sort of fad to hybridize pelargonium species, so that, for instance, the *Geraniaceæ* of Sweet (1820-1830) contain almost 500 of such artificial hybrids, whose origin already at that time had been partly unknown. In the course of time, the origin of each cross became more and more obscure, so that at the present time we are unable to determine the exact origin of a large part of the pelargoniums found in our botanical gardens. This is especially the case in regard to the species which were called lemon-geraniums as early as the time of Sweet, and with which the rose-geranium must be included.

Andrews, in his *Geraniums* (1805), gives under the name of *Geranium capitatum et varietas* a table containing two pelargoniums, one of which is closely related to *Pelargonium capitatum* and perhaps identical with it. The other variety, however, seems to be related to the rose-geranium. The species represented in his plate bears the name of *rose-scented geranium*, the variety that of *Otto of roses*, a name probably due to the mistake of a gardener. It is not impossible that the latter had been one of the original plants of

our rose-geranium; but I am not sure how great the influence of *P. capitatum* was in the creation of this variety. In the work quoted, there is found also another pelargonium closely related to the above-mentioned variety and to *P. capitatum*, and which bears the name of *P. oxoniense*, because it had first been cultivated in Oxford, England. It is very probable that the parent plant of the rose-geranium was originally purchased under the name of *Oxoniense roseum*, and that this name came to be misunderstood in the course of time. At any rate, from what has been said it follows clearly that the parent plant was an English product, perhaps from Oxford, that it is related to *P. graveolens*; perhaps also to *P. capitatum*, and that it was well known as early as 1805 on account of its rose-odor.

It is, furthermore, of interest that in the above-mentioned book there is a plate representing an hybrid of *P. graveolens* with *P. capitatum*, which likewise is related to the rose-geranium, and which has variegated leaves. Andrews classified it as *G. capitatum* var. and says that the influence of *P. quercifolium* changed *P. capitatum* in such a manner as to cause the confusion of *P. quercifolium* and *P. graveolens*. It is very interesting that in the work of Sweet neither the name of *P. graveolens* nor that of rose-geranium can be found.

From all this it can be seen that there exists no botanical name for the plant. In literature the name of *P. roseum* Willd. is often found. In the herbarium of this author there are two identical plants which bear the names of *P. radula* var. *roseum* and of *P. graveolens* var. *roseum*, both corresponding to the description of Willdenow in *Spec. pl.* III (1800), page 679, which is given there under the name of *P. radula*  $\beta$  *roseum*. This plant, according to his own words, is a hybrid of *P. radula* and *P. graveolens*, an opinion which seems to be justified. But it is hardly identical with the rose-geranium, as I was inclined to believe before this.<sup>1</sup>

It is probable that in France, besides the rose-pelargonium, there is cultivated, though to a smaller extent, *P. odoratissimum* (L.) Ait. and *P. fragans* Willd., as indicated by Heuzé (p. 306). Both plants are different from the rose-pelargonium and of a delicate texture. *P. odoratissimum* belongs to the section of *Peristera* and was introduced into England, according to Sweet (p. 299), in 1724. *P. fra-*

<sup>1</sup> I dedicate this interesting plant (*P. Krappeanum* = *P. graveolens* Ait. hybrid.) to my friend, Dr. A. H. Krappe, of Indiana University, to whom I am indebted for valuable service in the composition of this paper.



gans is a hybrid of *P. odoratissimum* and the perennial *P. exstipulatum*, and in its appearance resembles the former species, but is perennial like the latter. Sweet (p. 172) says that it is an old plant of the English greenhouses. I have never seen these plants in the open or in a herbarium. In Algeria and Réunion the two species are certainly not cultivated.

#### MORPHOLOGICAL CONSTITUTION OF THE GLANDS.

The oil is furnished by the glands of the plant. These are found, as in all pelargonium species, in the green parts, especially on the surface of the leaves, where they are shorter than on the stem and the peduncles. In most cases they are from  $\frac{1}{15}$  to  $\frac{1}{18}$  mm. long and can be seen with the naked eye. They consist of from one to three small cylindrical base-cells and a small globular head. The number of the base-cells is smaller in the gland hairs of the leaves than in those of the stems. All gland hairs originate in epidermical cells which multiply by cross-division. The uppermost of the two cells rounds itself and becomes a small head. Whenever the gland hair possesses more than one base-cell, the latter is once more divided into two. The spicate head is, therefore, older than the next lower, and the lowest is the youngest. The oil is mostly found only in the small head, rarely in the neighboring cell. When young, the end-cell is colorless; later it is colored by a yellowish substance and finally becomes brown. This substance often forms a globular body, which, according to Weiss (pp. 577-599), who obtained this result in a related species, lies at the bottom of the cell and is surrounded by a clear liquid. Of the numerous chemical reactions I might mention that of iodine, which colors the young small head bright yellow, the older one dark yellow or almost brown. A solution of potash-lye (KOH) gives a yellow color. Chloride of iron brings about the reaction of tannin.

The researches of Behrens (*Ueber einige aetherisches Oel secernierende Hautdrüsen* in den Ber. d. deutschen Bot. Ges., IV, 1886, p. 400), which this author made in the glands of *P. zonale*, do not completely agree with those of Weiss. According to the former, the oil originates in the plasma of the cell, so that, upon adding alcohol vacuoles may be seen. In a later state the oil lies in the form of a meniscus between plasma and cell-wall. Finally, there is found between plasma and oil a stratum of cellulose, which changes into a

cuticle. De Bary (*Vergl. Anatomie*, pp. 93-105), had supposed, before the experiments of Behrens, that the oil originates between the cuticle and the other stratum of cellulose, and then enters the plasm; an opinion which, according to Behrens, is wrong.

Concerning the situation of the gland hairs, there exist different opinions, which do not correspond to reality. Charabot and Laloue (*Comptes rendus*, CXXXVI, 1903, p. 1467) say that only the leaves contain oil, and that in the stems, petioles and flowers, no oil can be found. From this they conclude that the chlorophyll is the origin of the oil.

According to Blandini, of the Agricultural School of Portici (Bertoni in the *Bull. de l'Off. du Gouv. de l'Algérie*, XII, 1906, p. 277), the flowers produce a larger quantity of oil of excellent quality, an opinion which is certainly not in accordance with the facts.

The oil glands are of great use to the plant, as they protect its vegetable parts from insects and snails. As a matter of fact, all pelargoniums are but little damaged by such enemies. It appears to me to be improbable that the exhalation of aromatic oil plays a part in equalizing the temperature in the neighborhood of the plant, as is often asserted.

#### GEOGRAPHICAL DISTRIBUTION OF THE ROSE-GERANIUM.

The cultivation of the plant arose in Southern France, spread from there to Algeria, and was then transferred to Réunion and later to Southern Spain. According to R. Gattefossé, insignificant centres of production are found in Corsica (cf. *Parfum. moderne*, III, 1910, p. 73); according to Heuzé, also in Turkey and Egypt, in which latter country the plant is called *yt'r beledi*, according to the same author.

In France the plant was first cultivated at Grasse, at the foot of the Maritime Alps, near Cannes. Though it was known there as early as 1819, it seems to have been grown only to a limited extent before 1847 (Charabot and Gatin, p. 289). According to the accounts of Grec (*Réveil agricole*, May 26th, 1901), the cultivation, once of considerable importance, had deteriorated in a regrettable manner. Immigrants transmitted the cultivation of the plant to Algeria, where it sprang up shortly after 1847. The plant was first cultivated in the district of Sahel, Western Algeria, between Oran and Mostaganem, afterwards in the plain of Metidja, near the town of Alger,

and in the litoral of the province of Constantine, near Philippeville and Bougie (Charabot and Gatin, p. 289). Exact accounts regarding the cultivation in the province of Alger are found in Ducellier. The amount of hectares under cultivation is as follows:

Rovigo,	} South of Alger in the plain of Metidja	250
Chebli,		210
Boufarik,		200
Bouira, 123 km. to the east of Alger,		160
Mouziaville, west of Blida,		45

Plantations are also found on the hills in the west and southwest of the town of Alger, at a small distance, near Staoueli, Rivet, Bourkika and Chéragra.

To Réunion the cultivation spread not before 1880. The mild climate of the island is well suited to the plant. There it is found in heights of from 400 to 1200 meters, where neither sugar-cane, manioc, nor vanilla (Cordemoy, pp. 170-171) can be grown. The cultivation was favored by the sugar crisis of 1904-1906. Until recent years the lease was such that the owner of the plantation received two-thirds, the farmer one-third of the net profit.

In the Spanish province of Granada, experiments were made regarding the cultivation of the plant about the year 1890. Two firms engaged in the distillation of the oil, producing about 300 kg. (Schimmel, Ber., 1896, p. 33). Although the quality of the oil was in part excellent (Schimmel, Ber., 1894, II, p. 22), the area of cultivation did not increase, owing to the competition of the products of the French colonies, but it is kept up to this day (Charabot and Gatin, p. 289).

Concerning the cultivation of the plant on the Isle of Corsica I have not been able to obtain information.

In the Jewish colonies of Asia Minor, Rischon le Zion and Petach-Tikwah, there are plantations which were founded by Baron Rothschild (cf. Ruppin, *Seifensieder Zeitung*, XLIV, 1917, p. 74, reference in Schimmel, Ber., 1917, I-II, p. 111).

Of the products mentioned the Spanish and the French oil are preferred; they are exported almost exclusively to France, America and Russia (Charabot and Gatin, p. 293). It has been proposed to cultivate the rose-geranium also in other countries; for instance, in Australia and Mexico (*Perfumery and Essential Oil Record*, III, 1912, p. 242). In Limaru, British East Africa, cultivation ex-

periments have been made with a variety of *P. radula* (*Perfumery and Essential Oil Record*, V, 1914, p. 423); but they have not been continued.

According to a notice of Bertoni (in the *Cultivateur ex. Bull. Off. Gour. gén. de l'Algérie*; cf. Schimmel, Ber., 1907, I, p. 45), the cultivation of pelargonium in Italy is inconsiderable in spite of the rising consumption in the tobacco industry and its importance for the manufacture of perfumes. I must confess that nothing is known to me about the cultivation of pelargonium in Italy or of its use in the manufacture of tobacco.

#### CULTIVATION.

The plant may attain an age of more than twelve years (Charabot and Gatin, p. 290). In cultivation, all plantations are renewed after from five to six years (Heuzé, p. 307). The plant is indifferent to great heat, but suffers if the temperature sinks to 2° or 3° C., so that a winter temperature of 5° C. may be considered the lowest limit of cultivation. Réunion and Algeria, whose average winter temperature is from 11° to 12° C., are therefore much more favorable to the cultivation of the plant than Southern France, where the plants must be renewed every year or else be protected from the cold. To grow exuberantly, the plant needs a quantity of rain of at least 700 mm., and a locality well exposed to the sun. Good artificial irrigation, as it exists in Réunion, increases the weight of the crop, but not the quantity of oil in tons. In France and Algeria, therefore, this method is not used, especially because the soil is soon exhausted and gets a firm crust, which at length does harm to the plant.

#### QUALITY AND CULTIVATION OF THE SOIL.

The rose-pelargonium prefers a soil which is well permeable and of silicious or silicious-clayish quality. As the plant is very sensitive to stagnant water, the soil must be perfectly level and deeply plowed, the plant being in need of good ventilation to grow well. By this method also the root-stocks of *Cynodon dactylon*, the most disagreeable weed of Northern Africa, are removed. After every cutting the rows are hewed through or slightly plowed. The quantity of manure and the manner of its application and distribution is of great importance. Concerning this we have some accounts.

Boutilly on Réunion (p. 179), for the conditions prevailing there, recommends an annual manuring of a ton of superphosphate

per hectare. He tries (see table below) to prove that lime is worthless (cf. columns 5-6 of the table) and chloride of potassium and nitrate of sodium prejudicial (columns 7-9) to the plant. De Villelè (pp. 218-219, 249-251), on the other hand, maintains that lime is an excellent manure for acid soils such as are frequently found in Réunion.

Kind of Manure, (According to Boutilly, p. 178)		Results of an are.				Total.
		1st ctg. Jan., 1895.	2d ctg. May- June, 1895.	3d ctg. Nov., 1895.	4th ctg. Mar., 1896.	
1. Superphosphate,	200 kg.	1.085	1.335	1.4	.51	4.33
2. Superphosphate,	100 kg.	1.065	1.405	1.3	.525	4.295
Nitrate of sodium,	50 kg.					
Lime,	50 kg.					
3. Superphosphate,	150 kg.	1.18	1.165	.925	.54	3.81
Chloride of potassium,	50 kg.					
4. Superphosphate,	60 kg.	.765	.995	.88	.49	3.13
Chloride of potassium,	50 kg.					
Nitrate of sodium,	20 kg.					
Lime,	70 kg.					
5. Lime,	200 kg.	.600	.99	.8	.485	2.965
6. Without manure,		.795	.635	1.	.31	2.74
7. Chloride of potassium,	200 kg.	.32	.67	.89	.44	2.32
8. Chloride of potassium,	150 kg.	.49	.8	.61	.325	2.225
Nitrate of sodium,	50 kg.					
9. Nitrate of sodium,	200 kg.	.615	.515	.855	.24	2.225

He sees a confirmation of his opinion in analysis. The good effect of superphosphate is due, in his opinion, less to the phosphate itself than to the sulphate of lime, which is mixed with it.

Belle, whose plantations are situated in France at Biot, Dépt. des Alpes Maritimes, recommends 800 kg. of superphosphate, 600 kg. of nitrate of sodium, and 400 kg. of chloride of potassium per hectare (Charabot and Gatin, p. 291).

Lecq and Rivière recommend 300 kg. of sulphate of ammonium, and 150 kg. of sulphate of potassium (Charabot and Gatin, p. 291).

Jolivet uses 300 kg. of superphosphate, 200 kg. of nitrate of sodium or, in place of the latter, 150 kg. of sulphate of ammonium, and 150 kg. of potassium (Charabot and Gatin, p. 291).

#### PROPAGATION.

The propagation is made by cuttings, as the plant is mostly sterile. I have found, however, wild specimens producing fruits in the outskirts of the town of Alger, near Maison Carrée. For the propagation the third cut is generally used, the autumn drivings,

especially, at a length of from 25 to 30 cm. The expense for one thousand cuttings varies from 0.6 to 2 francs.

A good cutting must have from 4 to 5 lateral buds. The larger part of the leaves must be removed, as otherwise the heat would harm them. The cutting must be done with a knife, not by breaking, for the quick production of a callus, as otherwise mould fungi enter the wound. The preparation of the cutting is, therefore, the same as with our *P. zonale*. In most cases they are put in boxes in such a manner that there is an interval between the plants of a row, amounting to 1 or 2 cm., and also between the different rows, amounting to 15 or 20 cm. The cuttings, well rooted, are put in the open land from 15 to 20 cm. deep and earthed up slightly. The distance between the individual plants varies. According to Charabot and Gatin (p. 292) there is, in most cases, a distance of from 30 to 35 cm. between the plants of a row, and one of from 70 to 80 cm. between the rows. On a hectare there may be, then, from 35,000 to 50,000 plants. Heuzé (p. 306) proposes from 40 to 50 cm. between the individual plants of a row, and from 65 to 100 cm. between the rows. The same author points out that in the plantations of Simonnet in Hussein Dey and of Chiris in Boufarik, a distance of 90 cm. between the plants and rows is used, so that the hectare contains from 10,000 to 12,000 plants. For the plantations of Mercusin in Chéragas and of Ferraud in Hydra, the distance between the plants and rows is 50 cm., and the total amount of plants is 40,000 per hectare.

#### DISEASES.

There are very few diseases from which the plant has to suffer. In its youth it is attacked by insects. In a full-grown stage, the oil is a good protection against insects and snails. *Cuscuta* does not do great harm to the plant. Then the shrubs must be cut away and the stumps sprinkled over with a liquid of 5 per cent. of iron-vitriol. Species of *Orobancha* may also sponge upon *pelargonium*. Of other weeds prejudicial to its growth, *Cynodon dactylon* L. may be mentioned.

#### HARVEST.

The plants well cultivated may reach the height of a meter, and in Algeria they are cut in the course of the hot season with a sickle, three or two times. The weather must be sunny and dry. At the first harvest, which generally takes place in April, the branches may

be shortened by 50 or 70 cm. In the second cut, which takes place in June, the branches are shortened by only 25 or 30 cm. Under good conditions there is a third cut in November. For only two cuts, the months of May and October are chosen. The branches are gathered in open baskets and vats, to avoid fermentation. The material must be worked up immediately. For distillation the leaves of the young shoots only are used. According to the accounts of Heuzé (p. 307), there may also be used leaves which have been carefully dried by turning. They are said to produce a better oil.

#### DISTILLATION.

Distillation is done in retorts with double bottom, to avoid irregular heating of the contents. In Algeria and Réunion almost every plantation has its own retort. The substance is distilled with water and produces an oil of yellowish, greenish or brownish color. In the Sahel of Algeria and the Metidja, there were, according to Heuzé (p. 308) about 48 retorts in the year 1893, producing annually 300 kg. of oil. According to Cordemoy (p. 171), there existed in Réunion about 250 retorts, every one of which yielded a tax of 10 francs.

Concerning the output of the harvest there are two accounts. According to Charabot and Gatin (p. 293) from 1000 to 1800 kg. of leaves yield, in Réunion, 1 kg. of oil. One hectare yields, in Réunion, from 30 to 50 kg.; in Algeria, from 20 to 30 kg. Heuzé (p. 307) relates that every individual plant yields 1 kg. of leaves, one hectare, consequently, 40,000 kg. But since 100 kg. of leaves yield only from 7 to 7½ g. of distillate oil, one hectare yields 400 times 7½ g., that is, 30 kg. of oil, a result which nearly agrees with the preceding. Plants of Southern France are said to produce less oil than those of Algeria.

#### PROCEEDS.

Charabot and Gatin (p. 293) publish two accounts for the year 1901.

Jolivet in Algeria calculates the annual expense per hectare in the following manner:

Cultivation and expenses of distillation,	300 francs
Annual amortization of the expenses,	60 "
Lease,	75 "
	<hr/>
	435 "

Schilling in Algeria comes to a similar result :

Lease,	60	francs
45,000 cuttings for 90 francs in 8 years,		
per year,	11.25	"
Plough,	20	"
Plantation,	30	"
Weed, twice,	40	"
Ploughing, twice,	20	"
Harvest,	120	"
Distillation,	182.50	"
Packing,	13.50	"
	<hr/>	
	497.25	"

To these expenses corresponds a revenue of 30 kg. of oil, each selling at 35 francs, that is, 1050 francs; the net proceeds per hectare amount, then, to 500 francs.

Grec (*Réveil agricole*, May 26th, 1901) estimates 40,000 kg. of leaves per hectare; according to him, 100 kg. yield a net proceed of from 5 to 5½ francs, so that a hectare would yield 2000 francs. This estimate seems to have been made for French plantations. There the expenses would naturally be greater than in Algeria.

#### EXPORTATION STATISTICS.

##### ALGERIA.

<i>Year.</i>	<i>Exportation in kg.</i>	<i>Price per kg. in francs.</i>
1888		64
1889		85
1890		55
1891		50
1892		50
1893		54
1894		53
1895		52
1896		49
1901	37,500	44
1902	35,300	41
1903	31,200	36
1904	53,600	34
1905	52,600	30
1906	54,600	25



<i>Year.</i>	<i>Exportation in kg.</i>	<i>Price per kg. in francs.</i>
1907	38,700	25
1908	46,600	22
1909	41,000	24
1910	33,800	30
1911	28,500	35- 60
1912	24,900	60
1913	38,400	70-100

The exportation of the Algeria oil to Germany, according to Schimmel (Ber., 1903, II, p. 31), in the year 1900 amounted to 1140 kg.; to France, to about 8300 kg., and to Italy to 105 kg.

RÉUNION.

<i>Year.</i>	<i>Exportation in kg.</i>	<i>Price per kg. in francs.</i>
1890		56
1891		44
1892		49
1893		46
1894		45
1895		46
1896		44
1897		38
1898	16,000	32
1899	13,000	30
1900	7,100	30
1901	15,000	40
1902	17,193	36
1903	25,323	29
1904	27,660	27
1905	38,334	24
1906	31,645	22
1907	31,247	21
1908	34,300	20
1909	57,580	20
1910	65,000	34
1911	45,000	
1912	43,000	70
1913	43,614	40
1914	70,000	77
Beginning of the war		25-20

(*To be Continued.*)

## THE ANALYTICAL CHARACTERISTICS OF POWDERED TALCUM FOR USE IN TOILET ARTICLES.

By GEORGE E. ÉWE.

Talcum is used for very many commercial purposes such as lubrication, as fillers in rubber and compositions of various kinds, paper, marking pencils, paints, the cleaning of textiles, for clarifying and absorbent processes, etc. The chief pharmaceutical uses are: for toilet talcum, medicinal dusting powders, face powders, foot powders, as a lubricant in tablet manufacture, for coating pills and as a clarifying and absorbent agent.

These many and varied uses call for various grades, and, as a consequence, the market affords many grades. Therefore the establishment of suitable standards for analytical characteristics for the proper selection of powdered talcum for use in toilet articles becomes a specific necessity in order to obtain satisfactory material.

Originally talcum is a rock, and being a natural product, is subject to all the variations in quality inherent in a product taken from the earth. In its natural location it is associated with many different kinds of mineral substances, all of which are harder than itself, talcum being practically the softest of all minerals. Therefore, in selecting talcum for toilet articles it is necessary that care be taken to insure the absence of these associated substances, which are harder, and as a consequence, harsher to the touch.

It is also important to take into consideration other characteristics, such as fineness of subdivision, whiteness, feel between thumb and forefinger, adherence, "pearliness," density, sifting quality, chemical characteristics and freedom from dampness.

Discussion of the importance of each characteristic and of the method of employing the characteristic as a means of selecting powdered talcum will be taken up in the case of each characteristic mentioned above.

*Harsh Associated Substances.*—The presence of these substances is usually made evident by the "thumb and forefinger" test, which consists of rubbing a pinch of the powdered material between the thumb and forefinger and carefully noting the "feel." The value of this test can only be appreciated after extensive comparative tests.

*Fineness of Subdivision.*—This characteristic is determined by comparative tests under the microscope. A powdered talcum which is coarser under the microscope will be harsher to the touch and unsatisfactory in the “thumb and forefinger” test. No definite standard of size of particle can be laid down; frequent comparative microscopic observations in conjunction with the “thumb and forefinger” test being required to demonstrate the value of the microscopic method of testing the fineness of subdivision.

*Feel Between Thumb and Forefinger.*—This is known as the “thumb and forefinger” test. The method of making this test is outlined above under “Harsh Associated Substances.” The pharmacist will realize the importance of this test when he recalls that the prospective customer when considering the purchase of a powdered talcum will invariably make this test either between the thumb and forefinger or between the palms of the hands after first ascertaining the odor of the powder. The perfuming of toilet talcums is foreign to the subject of this article but must be considered of even more importance than the analytical characteristics of the powder used in making the product, provided the powder passably conforms to the analytical tests.

*Whiteness.*—Whiteness, to a certain degree, is measured by fineness of subdivision; the finer the subdivision the whiter the powder. This is only true, however, of talcum from the same natural source. The comparative color of talcums from different sources must be considered a separate problem. Whiteness is best determined comparatively by placing a small mound of the powder under test on a white sheet of paper and comparing its color with that of a similar mound of a satisfactory standard powder on the same sheet of paper. Whiteness of product is a very important matter, as the trade prefers a snowy-white product.

*Adherence Test.*—A desirable characteristic of toilet talcum consists of its ability to adhere well to the skin when rubbed thereon, because one of the reasons for the use of talcum is its covering power. Aside from this, toilet talcum must adhere well from the standpoint of economy, the more adherent product possessing greater covering power and therefore requiring the use of less material for a given amount of surface. The adherence test can be applied by rubbing the talcum upon the under side of the

forearm or other smooth, non-hairy surface, in comparison with a satisfactory standard product. Considerable experience gained through numerous comparative tests is necessary in order to develop a standard and demonstrate the value of this test.

*"Pearliness."*—"Pearliness" is one of the desirable qualities of a toilet talcum. It consists of the ability of the product to produce a pearly or wax-like "bloom" on the skin. Powdered talcum produces this effect by breaking up the reflection of the light which approaches total reflection from a shiny skin. This it does by superimposing innumerable minute reflecting surfaces over the single, almost continuous, reflecting surface represented by a "shiny" skin. The test for "pearliness" is made at the same time as the adherence test, and like the adherence test, considerable experience with it is required to demonstrate its value and to develop a standard.

*Density.*—"Fluffiness," or low density is desired by an average user of toilet talcum. Powdered talcums vary considerably in this respect. These variations are due to differences in chemical and physical characteristics of the rock and the fineness of subdivision, adhering ability and moisture content of the powder. Maximum fluffiness is desirable, therefore, a standard method of testing for density and an arbitrary standard, based upon examination of satisfactory materials, must be established. The method of testing for density which has given excellent results in the laboratory with which I am connected, consists of determining the weight of the powder which is held by a standard size cup when the cup is filled with powder under specified conditions. For this purpose a small, cylindrical, metal crucible is used; metal being preferred to glass or porcelain for the reason that breakage would necessitate the extra trouble of determining a new standard. This metal crucible or cup is used as follows: The cup is weighed, the powder is poured in until it is piled up over the top; the excess is scraped off with a spatula and the crucible, so filled, is weighed again. As an arbitrary standard we have adopted a powdered talcum of which our cup holds 9 grams, having determined that such a talcum will possess a desirable "fluffiness." In making the determination of density care must be taken not to shake or tamp down the powder since the object of the test is to determine the density or fluffiness of the powder in a loose condition such as exists during its practical

use. The powdered talcum offered for use in the manufacture of toilet talcum varies considerably in "fluffiness." A recent examination of five lots from different sources showed densities of 10.4, 9.09, 9.36, 9.0 and 9.72 respectively when tested with the standardized cup described above.

*Sifting Quality.*—This is important because of the necessity of sieving powdered talcum owing to the presence of particles of extraneous matters and unground talcum in commercial shipments.

Sifting is also necessary in order to disintegrate lumps. The sifting quality is also important from the standpoint of ease with which it can be shaken from the market container of toilet talcum, in which it is finally used. Commercial talcums vary greatly in their sifting qualities, some lots being very difficult to handle because of their tendency to clump up and thus refuse to pass through the sieve. Considerable expense and trouble can be eliminated by careful selection of powdered talcum in this respect. The fineness of subdivision, density, adhering ability and moisture content all influence the sifting quality of a powdered talcum.

*Freedom from Dampness.*—Freedom from dampness is necessary as affecting chiefly the sifting qualities; dampness rendering sifting very slow and tedious. Dampness also affects the color and density, both of these characteristics being deleteriously altered. No exact figure for maximum moisture content can be laid down as satisfactory for all lots of talcums, but in most cases not more than 3 per cent. of moisture should be lost by powdered talcum when dried at 100°C. to constant weight.

*Chemical Characteristics.*—Talcum is essentially a native hydrous magnesium-aluminum silicate, but may be associated with numerous other substances. The chemical characteristics of talcum and associated substances materially affect the physical tests discussed above but any baleful influences may be avoided by selecting material in strict accordance with these physical tests.

As a matter of fact, it is only by the application of the careful analytical tests mentioned in this communication that a high-grade toilet talcum can be produced.

PHARMACEUTICAL RESEARCH LABORATORIES,  
H. K. MULFORD COMPANY,  
PHILADELPHIA, PA.

THE VOLATILIZATION OF ETHYL NITRITE FROM  
SWEET SPIRIT OF NITRE.

BY J. G. ROBERTS.

An investigation to determine the cause of the deterioration of sweet spirit of nitre was instituted on account of the frequent prevalence of low strength samples, which had supposedly been stored under normal conditions.

As shown by the following results deterioration is due to either the decomposition of, or, to the volatilization of the ethyl nitrite. Decomposition is due to the action of light and volatilization to the action of heat, to the imperfect sealing of containers or to insufficiently filled containers. Carelessness or slowness in mixing the ethyl nitrite and alcohol is also a contributing factor. The latter cause can however be eliminated, particularly when a small quantity is prepared, by using the sealed tubes which contain sufficient ethyl nitrite, which when mixed with one pint of alcohol will produce sweet spirit of nitre of normal strength.

Ethyl Nitrite or Nitrous Ether, as it was first named, is a well-established product which has been well known for a considerable period. It was discovered by Kunkel as early as 1681, and was obtained by the reaction of nitric acid, alcohol and copper. It is a yellowish volatile liquid of a pleasant, ethereal odor, has a specific gravity of .990 at 15.5° C., and boils at 17° C. It is readily miscible with alcohol, from which it is easily dissipated when not properly stored.

In the present method of manufacture, ethyl nitrite is produced by the reaction of sodium nitrite, sulphuric acid and alcohol. It is preferably made in a stone-ware vessel of convenient size, which is provided with a mechanical stirrer. The resulting gaseous ethyl nitrite is passed through a well-cooled condenser and collected in an ice-packed receiving vessel. As it is decomposed in the presence of water, particular care is taken to render it anhydrous.

Sweet spirit of nitre is a very popular article, and judging from the attention given it, it has the greatest popularity among the various National, State and Municipal authorities who have made it a very frequent cause of investigation and examination. That their vigilance is justified is proven by the large number of cases of low quality sweet spirit of nitre that they have found. The ready vola-

tility of its ethyl nitrite content, has always been a disturbing factor, and is a matter of deep concern to all those who take pride in the quality of the preparations they dispense.

According to modern chemical classification ethyl nitrite is an ester and not an ether. Its ethereal quality was probably the reason for the name or possibly on account of the discarded, inaccurate term "compound ether," that was formerly applied to this class of products. This inaccuracy should be corrected in the next revision of the U. S. P., and the name Spirit of Ethyl Nitrite adopted. It would then be consistent and in uniformity with Spirit of Glyceryl Trinitrate, which has been adopted for spirit of nitroglycerine.

With the object of determining the factor most responsible for the deterioration in quality, a number of experiments were conducted and the following results noted:

#### EXPERIMENT NO. 1.

One-ounce flint and amber bottles were completely filled and placed in a refrigerator.

	<i>Flint bottle.</i>	<i>Amber bottle.</i>
Original strength,	5.25 per cent.	5.25 per cent.
After keeping 4 weeks,	5.22 " "	5.23 " "

Practically no change occurred in contents of either style of bottle when kept for this period under the above condition.

#### EXPERIMENT NO. 2.

One-ounce flint and amber bottles were completely filled and kept in a dark closet at room temperature for four weeks.

	<i>Flint bottle.</i>	<i>Amber bottle.</i>
Original strength,	5.25 per cent.	5.25 per cent.
After keeping 4 weeks,	5.20 " "	5.19 " "

Very little change occurred in contents of either style of bottle.

#### EXPERIMENT NO. 3.

One-ounce flint and amber bottles were completely filled and kept on shelf for 4 weeks.

	<i>Flint.</i>	<i>Amber.</i>
Original strength,	5.25 per cent.	5.25 per cent.
After 1 week,	5.24 " "	5.25 " "
After 2 weeks,	5.24 " "	5.23 " "
After 3 weeks,	5.24 " "	5.22 " "
After 4 weeks,	5.07 " "	5.19 " "

Only a little change occurred in the amber containers and practically none in the flint containers until between the third and fourth weeks, when a perceptible decrease in strength occurred. This peculiarity has been noted at various times and may be due to the presence of a foreign substance.

## EXPERIMENT NO. 4.

One pint was placed in a one-pint glass stoppered bottle and examined weekly.

*Original strength. After 1 week. After 2 weeks. After 3 weeks.*  
5.25 per cent.      5.1 per cent.      4.99 per cent.      4.96 per cent.

*After 4 weeks.*  
4.86 per cent.

This bottle was kept on a shelf under ordinary conditions. A progressive loss of about .4 per cent. for this period is noted.

## EXPERIMENT NO. 5.

A one-quart cork stoppered bottle was filled and placed on shelf. Two ounces were taken out each day and the strength noted. The following results given in the order of their testing, were obtained on succeeding days: 5.22 per cent., 5.22 per cent., 5.22 per cent., 5.18 per cent., 5.16 per cent., 5.1 per cent., 5.07 per cent., 5.11 per cent., 5.01 per cent., 4.95 per cent., 4.90 per cent., 4.7 per cent., 4.57 per cent., 4.62 per cent., 4.04 per cent. As the original strength was 5.25 per cent., it is shown that a loss of 1.21 per cent. was suffered during that period. This test was conducted in order to parallel the conditions that exist when a large number of orders are filled from the same container.

## EXPERIMENT NO. 6.

Four ounces were placed in a pint bottle and kept on a shelf under ordinary conditions.

*Original strength. After keeping 1 day. After keeping 21 days.*  
4.58 per cent.      3.92 per cent.      2.71 per cent.

The loss of 1.87 per cent. of ethyl nitrite during this period shows the inadvisability of placing a small quantity in a container that allows a large air space above the liquid.



EXPERIMENT NO. 7.

One-ounce bottles were completely filled, then exposed to direct sunlight, and assayed weekly.

	<i>Flint.</i>	<i>Amber.</i>
Original strength,	5.25 per cent.	5.25 per cent.
After 1 week,	4.10 " "	5.24 " "
After 2 weeks,	2.62 " "	5.20 " "
After 3 weeks,	1.89 " "	5.18 " "
After 4 weeks,	1.18 " "	5.19 " "

Results show surprisingly little change in the contents of amber bottles and that the contents of the flint bottles show marked deterioration.

EXPERIMENT NO. 8.

Desiring to determine the relative volatility of ethyl nitrite and alcohol when in admixture, 16 ounces were heated on a steam bath. When a quantity equal to the amount of ethyl nitrite present had been driven off it was found to contain 2.5 per cent. ethyl nitrite, which was a loss of 2.08 per cent. Upon continuing the evaporation until all of the ethyl nitrite had been eliminated, it was found that 2.5 ounces had been vaporized, about 1.75 ounces of which was alcohol.

EXPERIMENT NO. 9.

Exposure to the atmosphere in a porcelain evaporating dish.

<i>Original strength.</i>	<i>After 1/2 hour.</i>	<i>After 1 hour.</i>	<i>After 1 1/2 hours.</i>
4.58 per cent.	1.4 per cent.	.275 per cent.	.038 per cent.

The pronounced volatility of the ethyl nitrite is well illustrated in this test, which shows the elimination of practically all of it in 1 1/2 hours.

EXPERIMENT NO. 10.

Exposure to the atmosphere and agitation in a porcelain dish.

<i>Original strength.</i>	<i>After stirring 1 minute.</i>	<i>After stirring 3 minutes.</i>	<i>After stirring 5 minutes.</i>
4.56 per cent.	3.58 per cent.	2.19 per cent.	1.54 per cent.
<i>After stirring 10 minutes.</i>	<i>After stirring 15 minutes.</i>		
.57 per cent.	.19 per cent.		

The rate of elimination was substantially increased by stirring as most of the ethyl nitrite was dissipated in 10 minutes and practically all in 15 minutes.

As a result of this study we find that ethyl nitrite is easily dissipated from an alcoholic solution; that the action of direct sunlight is very destructive to it in flint glass containers; that partly filled containers are objectionable, and that it is bad practice to dispense numerous orders from the same container. The ideal method of storage is in small *completely filled*, amber bottles, kept in a refrigerator or ice-box.

NOTE.—Credit is to be given to Mr. T. R. Singer, for his valuable assistance in securing much of the experimental data herewith recorded.

ANALYTICAL LABORATORY OF SMITH, KLINE & FRENCH  
COMPANY.

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### ECHINACEA—A REPLY TO DR. BEAL.

The benefit to the scientific world which accompanies a wide discussion of experimental data can hardly be overestimated. Such debate uncovers many diverse opinions and often develops new and important avenues of thought. It stimulates the deductive faculties and should result in increased logical power. Facts are facts; they stubbornly resist controversion; but conclusions which may be drawn from facts are quite a different matter and too often depend upon the *a priori* considerations and unconscious prejudices of the one who is considering the data in question. This is, of course, a well-recognized danger among scientific workers and one against which every precaution is taken. In spite of safeguard, however, it may happen that the same set of data will indicate quite different underlying truths to two different observers and this is especially to be expected in cases where the data is considered by men of different training or different methods of arriving at experimental results.

The comment of Dr. Beal<sup>1</sup> upon our "Experimental Study of Echinacea Therapy,"<sup>2</sup> opens a discussion of the data which we obtained and the conclusions which we drew from them. Dr. Beal

<sup>1</sup> This JOURNAL, 93, 229 (1921).

<sup>2</sup> J. Agric. Res., 20, 63 (1920).

regrets, as we do, that only an abstract of the paper was published in this JOURNAL. It may be said here that the first idea was to reprint the paper in this JOURNAL and that the abstract was prepared only when it became apparent that space could not be given the longer article. The writers, however, have at their disposal a limited number of reprints of their paper and will be glad to furnish copies to those who apply for them as long as their supply lasts.

Dr. Beal has adopted the statistical method in analyzing our data. There can be little objection to this procedure when applied to data of the physical sciences; the law of averages, the method of least squares, and the theory of probability are of great service in such a connection. But when there is a question of animal experimentation—biological science—the great number of factors which enter into the case renders mathematical treatment uncertain unless there is a very large number of experiments upon which to base conclusions. Of these factors only a few can be evaluated; the larger portion are beyond control. Fortunately, however, it is possible to control within narrow limits the factors which are of importance in most investigations and the only untoward result that is due to the minor uncontrollable factors is some small variability in the behaviors of the animals.

The number of experimental animals which we used was small because, as we stated in the published account, the definiteness of our results did not seem to warrant a further sacrifice of animals and because we obtained no evidence which would sanction a hope that data derived from a larger number of experiments would controvert the conclusions that we arrived at with the data actually obtained. Dr. Beal has, however, indicated other conclusions which he thinks a clinician might fairly draw from our figures. These we purpose to consider in detail.

*Tetanus.*—Twenty-nine animals were given the toxin. Nineteen were given echinacea preparations, four were given the same strength of alcohol as those animals received which had been given the "Specific Medicine Echinacea," and six control animals were untreated. All of the animals died. Of the controls three died in two days and three were found dead on the morning of the third day. Of the experimental animals four which received each 7 ml. of remedy died in two days; five received 4 ml. of remedy and of

these one died in two days, one in four days and three in three days; five which received 2 ml. of remedy were found dead on the morning of the third day; five which received 1 ml. of remedy died on the third day. Of four animals which received each 1 ml. of 69 per cent. alcohol intramuscularly two died in three days and two in four days. All of the animals were carefully autopsied and none showed anything but the tetanus picture.

Dr. Beal has averaged the survival period of the nineteen animals which received echinacea preparations and has compared this figure with the similar average from the six controls. He finds 0.4 day in favor of the echinacea animals. The average of the animals treated with alcohol is 3.5 days, or 0.85 day better than the figure adduced for the echinacea. If the data is significant at all, and we think that a few hours or even days is hardly of importance in the face of the general fatal termination of all the animals, the only conclusions which an unbiased clinician could validly draw would be that the more echinacea the animal receives the sooner will he die; that alcohol may postpone the fatal issue of tetanus but cannot cure it, and that any apparent postponing of the death after echinacea treatment is due to the alcoholic content of the remedy used rather than to any inherent curative powers of the echinacea itself.

An instance of the variability which is encountered in this sort of work and the very minor importance of it may be found in the admirable paper of Doctors Rosenau and Anderson,<sup>3</sup> "The Standardization of Tetanus Antitoxin" from which the following is taken. Of fifty-eight guinea pigs<sup>4</sup> which were given the same dose of tetanus toxin subcutaneously all died; the first died in two days and twelve hours, the last in seven days and twenty-three hours; statistically:

Died in from 1 to 2 days, none				
2 to 3	"	3	or	5.1% of the total
3 to 4	"	22		37.9%
4 to 5	"	23		39.6%
5 to 6	"	7		12.0%
6 to 7	"	2		3.4%
7 to 8	"	1		1.7%

<sup>3</sup> Hygienic Laboratory, Bulletin 43, March, 1908.

<sup>4</sup> Table No. 4, pp. 16-17.

Of forty-two guinea pigs<sup>5</sup> which were given the same doses of tetanus toxin and tetanus antitoxin, the first died in two days and twenty hours; the last in six days and nineteen hours.

*Botulism.*—Five animals were given the culture. Three were treated with echinacea and two were reserved as controls. The controls died in one and three days, the treated animals in one, three and three days. The average, of course, favors the echinacea probably because there were not three controls. It is significant, however, that no control died before a treated animal and no treated animal survived the controls.

*Septicemia.*—The experimental work here is complicated by the well-recognized resistance of the guinea pig to subcutaneous infection by the hemorrhagic septicemia organism and on this account non-varying results were not expected. The experiment was only undertaken through the great desire of the authors to test the remedial value of the echinacea against a septicemia or what in common parlance would be termed a "blood poisoning." The results demonstrate the expected variations. Of thirteen animals which were given the culture, all became sick, eleven died and two recovered. Of the controls, one survived and two died in three days; of the animals which were treated with echinacea two died during the first day, two on the second day, two on the third day and of the remaining four one recovered, and the others died in five, six and twelve days. Thus, 40 per cent. of the treated animals had died before any of the controls, and 60 per cent. of the treated animals were dead when 66 per cent. of the controls had died. Furthermore, the five animals which are grouped in experiments 1 and 3, and of which four survived the controls (one recovering) had received no echinacea for eleven days before the injection of the virulent culture. What the meaning of the survival in the last case is we do not know, but we are certain that an average of such data is not only meaningless, but is actually misleading.

It is to be observed that 33 per cent. of the controls recovered without treatment, while but 10 per cent. of the treated animals survived; would the clinician argue therefore that it is better not to treat this disease since more cases recover without treatment than with?

<sup>5</sup> Table No. 2, pp. 9-10.

Dr. Beal states, "the average clinician in reviewing the results would be likely to claim that they showed a decided effect of the drug in prolonging the life of the infected animals." We are unable to agree with this statement. In the first place no such effect is demonstrated; in the second the clinician would be apt to attach great importance to the fact that the death of 40 per cent. of the cases was apparently hastened by the administration of the echinacea.

*Anthrax*.—The only point to note here is that the controls died in four and eight days, the average of which is six. We think that the average figure 6 is not significant.

*Rattlesnake Venin*.—Of eleven animals, six were treated, three were used as stated controls, and two others which were used in determining the M.L.D. of the venin were treated exactly as the controls and may be considered as such. One treated animal managed to survive after hovering between life and death for several weeks in a miserable condition; all of the others died. It has been stated somewhere that 80 per cent. of people bitten by rattlesnakes recover.

Of the fatal cases which received treatment one died on the first day, three died on the third day, and one died on the fifth day. Of the controls, two died on the second day and three on the third day. We do not think that the data warrants any favorable consideration of echinacea as a remedy in crotalus poisoning.

*Tuberculosis*.—Of eight animals which were infected with the organism two were kept as controls and the rest were treated. One of the controls died in thirteen days; the other control died on the thirty-third day, when four of the treated animals had succumbed, and was survived by the two remaining treated animals for three and five days. Here again we have compared an average of six results with that of two results, which is hardly admissible. If two analyses of some substance showed 13 per cent. and 33 per cent. of, let us say, iodine, would it be legitimate to state that the substance contains 23 per cent. of iodine? The significant fact of the tuberculosis experiment is that, in spite of the fact that the animals received large amounts of the remedies and were given every favorable opportunity for recovery, every one of them died. Furthermore, if anyone wishes to sustain the contention that the slight survival period of the treated animals over the controls is really germane, he must be pre-

pared to show that this effect was not due to the continued ingestion of small amounts of alcohol which, it is said, is of value in tuberculosis.

*Trypanosomiasis.*—What has been said in respect to tuberculosis applies equally to the dourine experiments. Two of the controls died before the decease of any of the treated animals, and two other controls survived all but one of the treated animals. The period of sickness was:

Treated animals, 48, 61, 64, 66, 71, 93 days.  
Controls, 17, 30 78, 79 days.

In other words, when 83.3 per cent. of the treated animals had died, 50 per cent. of the controls were still living.

We cannot accept the idea that an unbiased clinician would draw other conclusions from these data than those which we have presented. Each of the writers has had considerable experience with clinical medicine; we are familiar with the reasoning of the clinicians and also with the great complexity and uncertainty of the evidence which they obtain. The great difficulty of the clinician is the lack of definite controls; he can seldom demonstrate that the patient would have died had he not received a certain treatment. On the other hand, it not infrequently occurs that a patient recovers when the physician had been certain that he would die. Under such circumstances there should not be any diversity of opinion between the clinician and the "laboratory worker." Each must recognize the limitations of his powers and opportunities and the evidence contributed by each must be given due consideration in determining the truth.<sup>6</sup>

After giving full and careful consideration to the comment of Dr. Beal, the writers wish to state that they see no reason to withdraw any of their stated conclusions, nor do they agree that the data can be construed to indicate anything in favor of the continued use of echinacea in these diseases.

LEIGH T. GILTNER,  
JAMES F. COUCH.

<sup>6</sup> In the published abstract the following corrections should be noted:

Page 227—For T. Giltner, read L. T. Giltner.

Page 228—Line 13, for "per se," read "per os."

## ECHINACEA.\*

In connection with the foregoing communication the following reprinted editorial is of considerable interest:

Intelligent members of the medical profession must be well aware that both the Pharmacopeia of the United States and the National Formulary, now recognized by Federal and State laws as standards for drugs and their preparations, include many products that can scarcely be justified as medicinal on the basis of scientific considerations. When once a preparation has found its way into these "official" lists, it thereby gains the presumption of some therapeutic virtue. All too frequently, what it lacks in this respect is replaced by the potent promises of specious advertising; and when the admitted product thus becomes recognized, its place often is long assured by some indefinable force of tradition and reverence for supposed pharmacopœial wisdom.

Among the products included in the National Formulary is the fluidextract of echinacea. The claims for this drug as an "alterative" and "antisyphilitic" are denoted by one of the publications of the American Medical Association as "extravagant and unwarranted," with the added statement that there are no established indications for its use.<sup>1</sup> In 1909 a report of the Council on Pharmacy and Chemistry of the American Medical Association denied echinacea a place in New and Nonofficial Remedies, with the statement that, in view of the lack of any scientific scrutiny of the claims made for it, echinacea is deemed unworthy of further consideration until more reliable evidence is presented in its favor.<sup>2</sup> Despite this, it is stated by experts of the U. S. Department of Agriculture that the use of echinacea has become extensive. The fluidextract and the tincture are made in enormous quantities, and the root enters into the composition of a large number of patent, proprietary and nonsecret mixtures. Couch and Giltner<sup>3</sup> of the Bureau of Animal Industry, who are responsible for this information, have collected details of the claims variously made for the drug. Echinacea is stated to be a corrective

\**Journ. of the Am. Med. Assn.*, 1921, 39.

<sup>1</sup> Epitome of the Pharmacopœia of the United States and the National Formulary, with Comments, Chicago, American Medical Association, 1916, p. 80.

<sup>2</sup> Echinacea Considered Valueless, *J. A. M. A.*, 53; 1836 (Nov. 27), 1909.

<sup>3</sup> Couch, J. F., and Giltner, L. T.: An Experimental Study of Echinacea Therapy, *J. Agric. Res.*, 20: 63 (Oct. 1), 1920.



of "depravation" of body fluids, and of septic, fermentative or zymotic conditions. It is said to antagonize infectious processes and "blood poison," and to be useful in puerperal sepsis, uremia, pernicious malarial or septic fevers, typhoid fever, and all fevers caused by absorption of septic material. It has been advertised as a specific against the venoms of rattlesnakes, other serpents, and insects. "Pyemia" "goiter," "smallpox," "anthrax" and "hydrophobia" are reported to have been cured by echinacea. It is alleged to be an antidote for tetanus. It has been used locally in erysipelas, bedsores, fever sores, chronic ulcers, glandular indurations, syphilitic nodules, burns and gangrene, and is to be an active sialogogue, diuretic and diaphoretic.

This is a rather formidable aggregation of potencies for even the most respectable of drugs. The government pathologists have accordingly undertaken to determine the possible usefulness of echinacea as a remedy in several pathologic conditions induced by bacteria, their products or allied toxins. The results of the experimental investigations on guinea-pigs are devoid of evidence of functional effects, as were the earlier studies of competent workers. In both tetanus and botulism produced by the administration of bacterial toxin, the course of the disease was not modified by the echinacea. In septicemia produced by injection of a culture of *Bacillus bovisepiticus*, and in anthrax produced by infection with *B. anthracis*, the result indicated that echinacea had no influence. In rattlesnake poisoning produced by injection of a solution of the dry venom, the echinacea preparations were without curative effect. In the chronic diseases, tuberculosis produced by injection of a human strain of the bacillus, and trypanosomiasis produced by injection of *Trypanosoma equiperdum*, the remedy was administered over an extended period of time without apparently influencing the course of these diseases. Of course, it will be retorted that the negative results on laboratory animals need not necessarily apply to sick human beings, and that subtle potent effects are not always discovered by research workers. An appeal may be made to the "generations" of patients, particularly American Indians, who have experienced the beneficent influences of echinacea. Scientific medicine of today, however, asks for evidence that can be demonstrated by the pharmacologist or can be appreciated and accepted by the critical clinician as well as the quack. Echinacea has not yet established its claims for such recognition although it may remain a name to conjure with.

## ABSTRACTED AND REPRINTED ARTICLES

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### THE ORIGIN, DEVELOPMENT AND VALUE OF THE THALLEIOQUIN REACTION.\*

By WM. BEAMONT HART, F. G. C.

An investigation as to the analytical value of the thalleioquin reaction was carried out by the author in the year 1909, but the results as to its quantitative value were of such a negative character that they were not considered to be worthy of publication at the time; in view, however, of later published work, they appear to have some importance.

The earliest published record of the green coloration produced by the addition to a quinine solution of chlorine water followed by ammonia is made by H. A. Muson (*Phil. Mag.*, 1835, 158), who gave its sensibility as 1 in 8750. In Merck's "Reagentzien Verzeichnis" Manson's reaction for morphine and quinine is mentioned, but from the description and references it is quite evident that the name "Manson" is a misprint for "Muson." Brandes and Leber, 1839, gave the name of dalleiochin or thalleioquin to the green product, hence the name of the reaction.

The reaction has been developed in various ways too numerous to detail here, by substitution of bromine for chlorine or by different methods of liberating halogen, to a sensitiveness of 1:20,000.

Attempts have been made to use this reaction for the colorimetric determination of quinine, using varying quantities of halogen for quinine molecule: Trimble<sup>2</sup> used 38 atoms of chlorine; Léger<sup>3</sup> used 13 atoms of bromine, and states that the method is useless; Vondraseck,<sup>4</sup> using potassium bromate and hydrochloric acid, assumed

\*Reprinted from the *Journ. of the Soc. of Chem. Industry*, 40:7; April, 1921.

<sup>1</sup> Flückiger, 1872; Vulpus, Vitali, 1886; Hyde, 1897, etc.

<sup>2</sup> Allen, "Comm. Orig. Anal.", 2nd ed.; vol 3, pt. 2, pp. 401-402.

<sup>3</sup> Léger, *J. Pharm. Chim.*, 1904, 281.

<sup>4</sup> Merck, Ann. Rep., 1908, 275.

that with modification and practice it could be used; LaWall used from 10 to 40 atoms of bromine from potassium bromate and hydrobromic acid per mol. of quinine.<sup>5</sup>

From the figures given by Trimble and Léger—the only data found up to 1909—it appeared that the amount of halogen used was excessive and variable. The present author therefore investigated the reaction to determine more minutely (1) the exact conditions necessary; (2) its limit of sensitiveness, and (3) if it were possible to brace a quantitative method on it, using bromine as the halogen.

The following solutions were used: (1) Quinine as sulphate, in dilutions 1:1000 to 1:200,000; (2) bromine water, freshly made, and (3) ammonia, 5 per cent. solution. Preliminary trials showed that the shade of color produced depended (1) on the quantity of bromine; (2) time of action of bromine before addition of ammonia, and (3) deterioration of color by standing after reaction is obtained.

*Quantity of Bromine.*—In all, eleven dilutions were treated with increasing amounts of bromine, starting with 0.75 and increasing by 0.75 up to 12.75 atoms per mol. of quinine, ammonia being added after similar times of actions, the solutions made up to a total volume of 25 c. c. or  $2\frac{1}{4}$  inches in the tube, and the color shade noted, with the following results:

With quinine solutions 1:1750 or stronger, and with 6 or more atoms of bromine per mol. of quinine, before ammonia addition, a yellow precipitate is obtained.

With increase of bromine and addition of ammonia the color proceeds from blue, blue-green to yellow-green and yellow; finally this yellow disappears, except in solutions 1:5000 or stronger.

The strongest color depth is obtained with 6 atoms of bromine shown consecutively in dilutions 1:1750 to 1:1,200,000; at 1:1000 this maximum appears somewhat earlier with 5.25 atoms of bromine, but the difficulty of comparing colors of precipitates may account for this.

The stronger the quinine solution, the earlier does the yellow shade of green appear; at 1:1000 to 1:10,000 it appears before and extends longer in the series after the maximum color is attained.

Contrary to a published statement that no green precipitate is

<sup>5</sup> LaWall, AMER. J. PHARM., 1904, 281.

obtained in quinine solutions of greater dilution than 1:1000, these results show at 1:5000, with 6 atoms of bromine, a decided cloudiness; at 1:2500, with the same amount of bromine, a precipitate; at 1:1750 this precipitation begins at 0.75 atom, is distinct at 2:25 atoms, and increases up to the addition of 6 atoms of bromine.

During the addition of ammonia, at dilutions of 1:1000 to 1:5000, a pink coloration is first obtained, which appears earlier with increase of quinine concentration; in every case, when the solution is alkaline, this coloration changes to green on standing.

With increase of bromine, at dilutions of 1:1000 to 1:5000, during addition of ammonia, white fumes appear, which with increase of quinine appear earlier in the series; these fumes were noted with bromine present to the extent of about 0.023 g. per 100 c. c. of solution in excess of the 6 atoms per quinine molecule.

*Time of Action of Bromine Before Addition of Ammonia.*—Experiments were now made to find the influence of definite intervals of time of action of bromine before addition of ammonia, the intervals chosen being immediate (five seconds), one minute, and five minutes, with the following results: with immediate action, and addition of ammonia till the solution is alkaline, the best results are obtained with stronger solutions down to 1:40,000, according to the amount of bromine present; with one-minute action weaker solutions give the best results; action of bromine for five minutes reduces the resultant color strength, but in the weaker solutions (1:40,000 downwards) this is still of deeper shade than with the corresponding dilutions with immediate action.

*Color—Strength Deterioration.*—Trials made for this purpose showed that the green colour fades to some extent, but not very materially, up to five minutes.

The following conclusions are drawn from the above results: (1) Excess of bromine and its prolonged action are detrimental to the production of the thalleioquin reaction, 6 atoms of this halogen for one minute being ample for strongest color depths; (2) with quinine solution 1:1000 to 1:20,000 the reaction commences in presence of 0.75, at 1:40,000 to 1:80,000 in presence of 1.5 to 2.25, at 1:120,000 in presence of 3, and at 1:200,000 in presence of 6

atoms of bromine per mol. of quinine; (3) as a qualitative reaction, by making a few preliminary trials it can be made very sensitive, the limit being 1 : 250,000 in a depth of liquid  $2\frac{1}{4}$  inches (of course, the greater the depth the greater will be its sensibility); for quantitative work, with so many variables, no credence of even approximate accuracy can be assigned to the reaction, except under very strict conditions and in very dilute solutions, as shown.

*Bromine Absorption in Aqueous Solution.*—Attempts were made to determine the bromine absorption of quinine in aqueous solution for 5, 10, and 20 minutes' action with 2.5, 5 and 11.5 tons of bromine per mol. of quinine, using quinine at 1 : 1000 and bromine water at one-tenth saturation, the excess of bromine being titrated with thio-sulphate after addition of potassium iodide. The results obtained showed that although 4 atoms of bromine appears to be the maximum quantity absorbed, and this is constant for five minutes, yet any excess over 2 atoms is only loosely held and appears to be slowly given up again.

The earlier workers (Andre, Brandes, etc.) did not find chlorine in their product; Commanducci,<sup>6</sup> by varying the time of action of chlorine, obtained two new red products even in alkaline solution—a statement at variance with the present author's bromine results. Comstock and Koenigs,<sup>7</sup> by extracting their quinine dibromide with water and separating by means of ammonia, did not obtain any thalleioquin reaction. Buraczewski and Dziurzynski,<sup>8</sup> on treating their quinine pentabromide with water not above 40° C., filtering and adding ammonia to the filtrate, obtained a white flocculent precipitate which soon became emerald-green and contained bromine, and they state that it is probably identical with the substance formed in the thalleioquin reaction. Christensen,<sup>9</sup> by progressive chlorination of quinine, obtained (1) quinine hydroxy chloride and dichloride, in which the vinyl group is saturated and which give the thalleioquin reaction when chlorine followed by ammonia is added to the slightly acid solution; (2) with 4 atoms of chlorine an unstable base, 5-chloro-6-

<sup>6</sup> Ber. Deuts. Pharm. Ges., 1915, 256; 1916, 247.

<sup>7</sup> Commanducci, Chem. Zentr., 1910, 1885.

<sup>8</sup> Ber., 1892, 1539.

<sup>9</sup> Anz. Akad. Wiss. Krakau, 1909, 333.

hydroxycinchonine hydroxychloride, which gives the thalleioquin reaction on treatment with an oxidising agent, a substance that combines with chlorine and ammonia; (3) with 6 atoms of chlorine, an unstable base, 5-dichloro-6-ketocinchonine hydroxychloride, which liberates 2 atoms of iodine from potassium iodide for the 1 active chlorine present, and therefore probably contains the group  $\text{—CO.CCl}_2\text{—}$  in the quinoline nucleus, with consequent conversion into the group  $\text{—C(OH):CCl—}$ . This base gives the thalleioquin reaction on addition of ammonia only; the green product on drying leaves a residue if chloro-5,6-diketohydroxycinchonine, the group  $\text{—CO.CCl}_2\text{—}$  being replaced, in presence of ammonia, by the  $\text{—CO.CO—}$  group.

As far as is known, then, the action of chlorine or bromine on quinine in dilute aqueous acidified solution is similar, and the products, beyond the dihalogen stage, that can be formed during or can give rise to the thalleioquin reaction, are numerous. The author attacked the problem from the analytical standpoint, and his conclusion, in 1909, that 6 atoms of halogen are required for the full reaction, is confirmed by the later results of Christensen; these also explain why, in the results of the bromine absorption in aqueous solution, apparently not more than 4 atoms as a maximum are absorbed, while actually 6 atoms take part in the reaction, the 2 atoms of iodine set free being determined as unabsorbed bromine. It follows, then, that quinine may be determined from its bromine absorption for five minutes in the manner stated:  $1 \text{ c. c. N/10 Br} = 0.0081 \text{ g. quinine.}$

It is possible and probable that the progressive halogen action runs concurrently to some extent; that is to say, part of the halogen is preferably used in further conversion of the intermediate products than in full conversion of quinine into intermediate products; this would explain why the thalleioquin reaction is obtained, though not to the full extent, by the action of much less than 6 atoms of bromine per mol. of quinine. Christensen's statement that the intermediate product, 5-chloro-6-hydroxycinchonine hydroxychloride, gives the reaction by treatment with an oxidising agent, a substance that combines with chlorine, and ammonia, may explain the mechanism of the delay in the final green color production by Vogel's reaction (1850), and also by Battandier's reaction (1904), since we

have the three essentials, time only being necessary; to some extent this also applies to Kletzinsky's reaction (1854), though in this case a further change probably occurs. During the early stage of this investigation the use of a solvent, such as amyl alcohol, for the green product suggested itself, but from the above results it was not thought to be of any value.

#### DISCUSSION.

The author, replying to a question, said that it was not practicable to estimate the color depths by the absorption spectra or by the colorimeter, owing to the rapid changes of color of the solutions and the large number of experiments being carried out at the same time.

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### THE QUINOTOXIN MYTH.\* †

TORALD SOLLMANN, M. D.

CLEVELAND, OHIO.

Some writers, especially in chemical and pharmaceutical journals, have attributed the toxic effect of quinine to the formation of a more toxic substance, "quinotoxin," or quinicin, as it is more properly called. This may be formed from quinine under suitable conditions, especially in the presence of free organic acids. It has been assumed that these conditions would arise in the stomach, and, also, that prescriptions containing quinine and an organic acid would be dangerously incompatible.

An examination of the data on which these assumptions were based reveals that these fears are not justified by the facts; that at most insignificant traces of quinotoxin could be formed in the body or be present in such prescriptions, and that the formation of considerable quantities would not be dangerous.

The error arose originally from exaggerated conceptions of the toxicity of quinotoxin, and was fostered by unproved assumptions as to the amounts that might be formed under practical conditions.

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†From the Department of Pharmacology, Western Reserve University.

## "QUINOTOXIN" A MISNOMER.

The name "quinotoxin" is probably in part responsible for the misconceptions. It is incorrect historically, suggests false theories, and leads to confusion with another, quite different, substance. It should be abandoned, and displaced by the perfectly good name bestowed on it by its original discoverer. Pasteur, in 1853, first prepared this substance and a corresponding derivative of cinchonin, and named them chinicine and chichonicine. The terms chinotoxin and cinchotoxin (and chinatoxins, collectively) were applied forty years later by Miller and Rohde,<sup>1</sup> who prepared these derivatives by a lightly different method. In this, they disregarded not only the fact that these substances had already received a name, but also the fact that the name chinotoxin had been applied eleven years previously by Ostermayer (1884) to an entirely different substance (diquinolin-dimethylsulphate). This is likely to lead to serious confusion. The anglicized terms of Pasteur will, therefore, be used exclusively in the following discussion.

## CHEMICAL RELATION OF QUINICIN AND CINCHONICIN TO QUININ AND CINCHONIN.

The structure of the cinchona alkaloids is not fully understood, as they have not been synthesized. It is fairly complex. That of quinin may be expressed as

$$\text{CH}_3\text{O} \cdot \text{C}_9\text{H}_5\text{N} \cdot \text{CHOH} \cdot \text{C}_9\text{H}_{14}\text{N}.$$

(a)      (b)      (c)      (d)

It includes a quinolin ring (b), to which are attached in the para position a methoxyl (a), and a pyridin derivative ("loipon") (d), through a CHOH linkage (c). Replacement of the methoxyl by other alkyl groups does not destroy the action, but may even fortify it (Fränkel *Arzeneimittelsynthese*). Omission of the group, however, greatly weakens the antimalarial efficiency, but increases the convulsive action. This is cinchonin,  $\text{H} \cdot \text{C}_9\text{H}_5\text{N} \cdot \text{CHOH} \cdot \text{C}_9\text{H}_{14}\text{N}.$

(a)      (b)      (c)      (d)

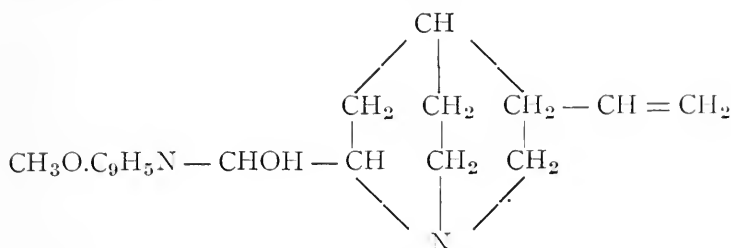
Replacement of the  $\text{CH}_3\text{OH}$  by OH gives cuprein.

Quinicin and cinchonin are formed when quinin or cinchonin are heated with acids. They have the same elementary formulas as quinin and cinchonin; but a rearrangement has occurred in the loipon and connecting link (d) and (c). It is generally believed that the

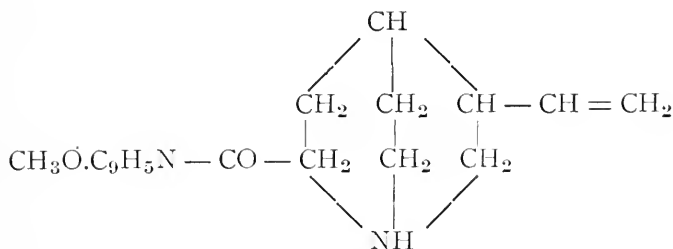
<sup>1</sup> Miller, W. von, and Rohde: *Ber. d. chem. Gesellsch.* 28: 1056, 1895.



linking CHOH in *c* is hydrolized to CO, the H being transferred to the adjacent C and N of the loipon, forming an imid group, and breaking the benzene ring, according to this schema :



(quinine) becomes :



(quinicin)

*Formation of Quinicin and Cinchoninic by Acids.*—Pasteur prepared quinicin by heating quinine with dilute sulphuric acid at 120 C. At 100, however, Biddle<sup>2</sup> found that dilute mineral acids (to normal) convert only from 2 to 3 per cent. of the cinchonine, while weak organic acid (acetic, etc., ten-thousandth normal) transform 95 per cent. The conversion is independent of the dilution or dissociation. Similar results were obtained independently by Rabe.<sup>3</sup>

At from 36 to 38 C. the conversion proceeds very slowly, even with organic acids, so that at most from 0.2 to 1 per cent. are converted in forty-eight hours. The concentration of cinchoninic probably does not increase with longer heating, for there is a parallel transformation of cinchoninic into an insoluble resin.

Some conversion into cinchoninic occurs also in sunlight, and

<sup>2</sup> Biddle, H. C.: J. Am. Chem. Soc. 34: 500, 1912.

<sup>3</sup> Rabe: Ber. d. chem. Gesellsch. 43: 3308, 1910.

more slowly in diffused light; but this also is converted into resin. The formation of cinchoninic or quininic may be judged by the dark discoloration (Biddle). Quinine behaves in all these respects essentially like cinchonine.

*Amount of Quininic Formed in the Stomach.*—Only insignificant traces of quininic could be formed in the stomach. The hydrolysis of quinine occurs, so far as known, only in acid mediums. This would confine its possible production in the body to the stomach. Kaufmann<sup>4</sup> found that traces of cinchoninic are formed by warming cinchonine with 0.1 per cent. hydrochloric acid. Biddle denies this, but suggests that the transformation would occur when organic acids are present in the stomach, as is not infrequently the case. Both writers overlook the time factor. They found only traces transformed after one or two days, whereas the quinine would remain in the stomach for only a few hours. They also overlook the fact that toxic effects of quinine occur at least as frequently if the quinine is given by channels other than the stomach.

*Formation of Quininic in Prescriptions.*—Biddle's work leaves no doubt that this would occur if quinine were subjected to prolonged boiling with organic acid; but there would be no occasion for this in prescribing. It would also be formed at ordinary temperature, but only very slowly; and its parallel conversion into insoluble resin would prevent its accumulation.

There is no doubt that solutions of quinine containing excess of organic acids would very slowly lose their activity, and, for this reason, old, discolored or precipitated solutions should not be dispensed; but there is no reason to apprehend danger from them. Even the changes occurring after a long time in capsules of acetylsalicylic acid and quinin hydrochlorid, as reported by Scoville,<sup>5</sup> are more important by the liberation of salicylic acid than by the formation of quininic.

*Actions of Quininic.*—Hildebrandt<sup>6</sup> asserted that this is not convulsive, that it has a digitoxin effect on the frog heart and that it

<sup>4</sup> Kaufmann, A.: Ber. d. chem. Gesellsch. 46: 1823, 1913.

<sup>5</sup> Scoville, W. L.: J. Am. Pharm. A. 4: 590, 1915; Bull. Pharm. 28: 527, 1915; *ibid.* 29: 174, 1915.

<sup>6</sup> Hildebrandt, H.: Arch. f. exper. Path. u. Pharmacol. 59: 127, 1908.

raises the blood pressure slightly. Biberfeld<sup>7</sup> found this toxicity for mammals quite low (lethal dose, 15 mg. per kilogram by vein; 200 mg. hypodermically, corresponding to about ½ ounce in man). In this large dose, it produced convulsions. It did not have a digitoxin effect on the exposed frog heart, but depressed it like quinin. It also depressed other smooth muscle; it produced local anesthesia similar to quinin, but was not antipyretic.

*Actions of Cinchonicin.*—The toxicity of this is also low. Hildebrandt found the hypodermic lethal dose as 150 mg. per kilogram for mice<sup>8</sup> (equivalent to 10 gm. for a man). The same dose of cinchonin was not toxic. Hunt<sup>8</sup> obtained about the same number for cinchotoxin (310 mg.) as for quinin (370 mg.). Rabbits seem considerably more susceptible. Biberfeld, minimum fatal dose, hypodermically, 10 mg. per kilogram; Fraenkel, fatal dose, hypodermically, 20 mg. per kilogram; Hildebrandt, cat, fatal dose, hypodermically, 20 mg. per kilogram. Death is preceded by violent convulsions.

Hildebrandt described a slight rise of blood pressure. Biberfeld found depression of the circulation. Fraenkel, in the exposed heart, observed first very strong contractions, then diastolic arrest.

#### CONCLUSIONS.

There is no occasion to fear toxic effects from the transformation of quinin into "quinotoxin" (more properly, quinicin). This substance is not especially toxic, and it could not be formed in significant quantities, if at all, in the body.

It may be formed in prescriptions containing quinine and organic acids; but this would proceed very slowly, and the quinicin would undergo further transformation into inactive products. Such solutions are perfectly proper if used within a few days. They should not be used after prolonged standing, when they become discolored and precipitated; not because they have become toxic, but because they have become inactive.

<sup>7</sup> Biberfeld, J.: Arch. f. exper. Path. u. Pharmacol. 79: 361, 1916.

<sup>8</sup> Hunt, Reid: Arch. internat. de pharmacod. 12: 500, 1903.

## PHARMACY AS A LEGITIMATE SCIENCE.\*

By DEAN CHARLES H. LAWALL,  
*Philadelphia College of Pharmacy and Science.*

Pharmacy as a legitimate and very important science should assume its rightful place in public esteem, according to Prof. Charles H. LaWall, Dean of the Philadelphia College of Pharmacy, which is celebrating its one hundredth anniversary.

The pharmacist must be educated in the basic sciences of botany, chemistry, pharmacognosy, physics and bacteriology, and this pharmaceutical education, begun in America one hundred years ago, has, in the opinion of Prof. LaWall, resulted in the formation of a class of men who deserve the respect and appreciation of the general public.

"The material changes which have taken place in our surroundings since the founding of the Philadelphia College of Apothecaries in 1821," says Prof. LaWall, "have been astounding. Epoch-making discoveries in medicine and chemistry have followed each other in rapid succession. New sciences, such as that of bacteriology, have arisen, and new remedial agencies, such as the serums and vaccines, have appeared, requiring highly specialized knowledge on the part of the dispenser as well as of the physician.

"I think it will be admitted without question that it is just as important to know how to fill a prescription correctly as to know how to write it correctly. Few but a trained pharmacist or a physician know how frequently the dispenser has the issues of life and death in his hands or how much care and skill are required in order to give and dispense medicines which shall be efficacious and safe. The making of even the simplest preparation demands an art and a technique acquired only by study and practice.

"It is necessary for the pharmacist to know the Latin name, the English name and the synonym or popular name of several thousand drugs, chemicals and medicines offhand, and also to know where to immediately turn for information which it would be folly to try to remember concerning these things.

"He must know the physical properties, such as appearance and solubilities of hundreds of chemical salts and to be able to apply distinguishing and identifying tests to substances concerning which there is doubt of their identity. He must know the doses of scores of drugs and medicines of high degree of potency and how to com-

\*Reprinted from *The Philadelphia Public Ledger*.

bine substances which are difficult of preparation in presentable and palatable form. He must know when comparatively harmless substances react to produce new products of poisonous possibilities. He must know the misleading, popular synonyms and use skillful and adroit methods in ascertaining from a purchaser just what is wanted when no prescription or written order is presented, for drugs having widely dissimilar properties often have the same name among persons of little education.

"In order to perform all these duties properly the pharmacist must be educated in the basic sciences of botany, pharmacognosy, chemistry, physics and bacteriology—pharmacy being a commingling of all these in a virtually applied form. That he may conscientiously fulfill these responsibilities and requirements he must, if he values his professional welfare and progress become a member of the professional associations representative of his calling and keep his scientific knowledge alive by constant reading and study.

"The pharmacist is the responsible authority under the narcotic and revenue laws for the proper handling and dispensing of habit-forming drugs and alcoholic liquors. The proportion of pharmacists who are recreant to this trust is small, indeed, compared to the great number who uphold the law. We hear very quickly about the violators, but nothing is said about the great army of those who are law-abiding. While the pharmacist seems to be fair game for would-be humorists in regard to the liquor question, jokes picturing him as a dope peddler or liquor dealer are as far-fetched and in as bad taste as the hoary jokes about the mother-in-law or sleepy Philadelphia.

"His is the privilege to deal in substances of interest, rarity and value, both intrinsic and potential. His wares are brought to him through the traffic lanes which cover the seven seas. From the spice-laden breezes of Oriental isles; from the base of snow-capped, majestic mountains of great continents; from icebound ports of the polar clime; from tropic jungles; from the land of the midnight sun; from the shadow of the pyramids themselves, come remedies whose history forms one of the most fascinating and romantic chapters of scientific study, for be it known that romance and sciences are often inextricably interwoven. Some of the preparations which he compounds date from the beginning of the Christian era; others had their own origin in some fortuitous discovery of a now forgotten and misled searcher for the philosopher's stone.

"'Your druggist is more than a merchant' is a slogan frequently seen nowadays. Think it over.

"The pharmacist is entitled to the respect of the community when he serves it faithfully, as is usually the case, and it is time that the same public-spirited support of the city, State and Nation is accorded to the institutions in which pharmacists are trained through-

out the land as is given to medical education and that they should be encouraged and aided in their laudable ambition to raise the educational standards and maintain this important calling at a point where it merits the dignity of a profession, the profession without whose intelligent service the practice of medicine would be hampered and its development retarded.

"Pharmacy is an art and a science. It can never be less; it should be more."

## DETERMINATION OF BISMUTH BY FORMALDEHYDE.\*

By S. B. TALLANTYRE.

The need for a rapid method of estimating bismuth in medicinal compounds suggested to the author of calling attention to the applicability of the formaldehyde reduction process. The details of the method are as follows:

The compound or preparation is warmed with a small quantity of dilute hydrochloric acid (about 10 per cent.) for a few minutes until it is decomposed and all the bismuth is in solution. The mixture can then usually be treated at once with a fair amount of formaldehyde solution, then a good excess of 10 per cent. sodium hydroxide, warmed and finally boiled until the precipitate of bismuth all separates to the bottom of the solution. The supernatant liquid is now treated with more of the reagents and the whole again heated to boiling to make sure reduction is complete. The clear liquid can then be decanted or filtered off and the bismuth either washed by decantation with hot, weak formaldehyde water, or if it is not in a well-coagulated condition, reboiled with a little more formaldehyde and sodium hydroxide solutions. By stirring or pressing the bismuth collects into a spongy mass which is very easily removed to a tared filter, Gooch crucible, or weighing bottle, washed with absolute alcohol, and weighed after drying an hour or so at 105° C.

The precipitate is pure bismuth produced according to the following reaction:



\**Chemist and Druggist*, through Merck's Report, April, 1921.

## MANUFACTURE OF ESSENTIAL OILS.\*

A preliminary statement of the general results of the 1919 census of manufactures, for the Essential Oil industry, has been issued by the Bureau of the Census, Department of Commerce, prepared under the direction of Mr. Eugène F. Hartley, Chief Statistician for Manufactures.

Reports were received from 78 establishments primarily engaged in the manufacture of essential oils (not including the synthetic or artificial oils) during 1919, with products valued at \$5,698,403. In addition, essential oils to the value of \$27,929 were produced by 7 establishments engaged primarily in other industries. The value of the natural essential oils for all establishments was \$4,439,704, and witch-hazel extract \$448,938. At the census of 1914 there were 107 establishments (inclusive of 2 primarily in other industries), with products valued at \$2,506,361, including essential oils \$1,289,482; witch-hazel extract, \$575,938.

In 1919, 29 establishments were located in Michigan, 22 in Indiana, 9 in Connecticut, 5 in New York, 4 in New Jersey, 3 in Pennsylvania, 2 in Virginia, and 1 each in California, Kentucky, Ohio and Tennessee.

The statistics for 1919 and 1914 are summarized in the following statement. These figures are preliminary and subject to such change and correction as may be necessary from a further examination of the original reports.

*Comparative Summary of Statistics for the Essential Oil Industry, 1919 and 1914.*

	Number of Establishments.		Production.	
	1919.	1914.	1919.	1914.
Value of Products.....	<sup>1</sup> 78	<sup>2</sup> 107	\$5,698,403	\$2,565,361
Essential Oils, Value .....	77	103	\$4,411,775	\$1,289,361
Witch-hazel Extract .....	3	11		
Gallons .....			125,412	917,690
Value .....			\$448,938	\$575,938
All Other Products, Value ..			\$837,690	\$699,941

\*From a report of the Department of Commerce, Bureau of the Census, Washington.

<sup>1</sup> In addition seven establishments engaged primarily in other industries made essential oils to the value of \$27,929.

<sup>2</sup> Includes two establishments which were engaged primarily in other industries.

## RHUS DERMATITIS.\*

Although the toxicology of poison ivy (*Rhus toxicodendron*) is fairly well understood, the toxic features of the related poison oak (*Rhus diversiloba*) have not been studied to comparable extent. For the harmfulness of the poison ivy, Pfaff<sup>1</sup> placed the responsibility on a substance isolated from the plant and named toxicodendrol. The latter is insoluble in water, but readily dissolves in the organic solvents like ether and alcohol. The product is so active that 0.005 mg. applied to the skin may suffice to provoke local symptoms with pain. A considerable latent period prior to the appearance of the cutaneous alterations has often been described. Recently McNair<sup>2</sup> has come to the conclusion that a polyhydrophenol, to which the name lobinol has been given, is responsible for the irritation of the skin caused by poison oak. The active substance is neither bacterial nor volatile. Poisoning occurs from actual contact with the resinous sap of the plant; but, as McNair points out, it may result through an intermediary agent, which carries the sap, such as particles of soot in smoke, clothing, cordwood, croquet balls and shoes. As in the case of all rhus dermatitis, the most common avenues of invasion of the poison are connected with the cutaneous surfaces, though the respiratory and alimentary tracts may also play a part at times in promoting intoxication with poison oak. The problem of latency has not been solved. With respect to the mechanism by which the dermatitis is spread so that it appears successively on different areas of the body, McNair has ventured several hypotheses. Thus, it may be due to (1) the direct transference of the poison itself by the fingernails or hands from one part of the body to another, or to new areas from the clothes or hair; (2) reflex irritation; (3) contiguity of tissue, and (4) varying durations of latency for the different skin surfaces on the body (varying with the respective thicknesses of their stratum corneum, chemical and physical differences in the skin, etc.). Perhaps further study will show an essential identity in the etiology of all forms of rhus dermatitis.

\* *Journ. Amer. Med. Assoc.*, 76: 18 (April), 1921.

<sup>1</sup> Pfaff, F.: *J. Exper. Med.* 2: 181, 1897.

<sup>2</sup> McNair, J. B.: *Pathology of Rhus Dermatitis*, *Arch Dermat. & Syph.* 3: 383 (April), 1921; *J. Am. Chem. Soc.* 43: 159 (Jan.), 1921; *J. Infect Dis.* 19: 419 (Sept.), 1916.



## ARSENIC FOUND IN PICKLES IS TRACED TO SECOND-HAND CONTAINERS.\*

As a result of two investigations recently made by the New York City Department of Health which revealed the presence of arsenic in a barrel of pickles and one of vinegar, a warning has been issued that all food dealers storing human foodstuffs in second-hand containers or vehicles which have been used for the transportation, storage or sale of poison, poisonous compounds or materials deleterious to human health, will be prosecuted to the full extent of the law. It was convincingly established that the arsenic did not originate in the foods in question, but these foods were permeated with it through the use of second-hand containers which had previously been employed for the storage of arsenic. An account of the cases, as described in the official Food and Drug Bulletin of the Department of Health, is given below:

"Recently, a complaint was received by the Bureau of Foods and Drugs indicating that several members of a family residing in the borough of Manhattan were suffering from food poisoning. An inspector of the Bureau was immediately detailed to make a thorough investigation.

"The inspector visited the home of the parents, and found that a mother and four children were suffering from the ingestion of dill pickles. Some of the pickles, which were still obtainable, were procured for the purpose of chemical analysis. It was learned that the pickles had been purchased from a pickle manufacturer doing business in this city.

"A thorough inspection was made of the factory in question, and a comparison made of the pickles found therein with those secured at the home of the persons made ill. A representative sample of the brine solution, and pickles contained therein was taken and submitted to the Chemical Laboratory of the Department of Health for analysis. By this analysis it was found that the brine and pickles contained large amounts of arsenic.

"Upon reviewing the developments of this investigation it was felt that the arsenic may have entered the pickles from the brine, which in turn had absorbed it from the barrel. The pickles were therefore transferred from the suspected container and the barrel removed to the Chemical Laboratory of the Department of Health, where it was scraped and the incrustations adhering thereto analyzed. The report of this analysis showed arsenic in large quantities. Fol-

\*From the *Spice Mill*, April, 1921.

lowing up on this investigation, the inspector of the Bureau of Food and Drugs learned that the barrel in question had been purchased from a second-hand barrel dealer in the borough of Brooklyn. Upon interviewing this dealer, information was obtained that the barrel in question had been purchased from a chemical company in Hoboken, New Jersey. An inspection was made of the chemical factory and it was found that the barrel in question had been used to transport crude arsenic from Mexico.

"In completing this investigation a condemnation of four hundred pounds of pickles was made at the pickle factory, and facts recommending prosecution of the pickle manufacturer were recommended for violation of Section 163 of the Sanitary Code, which states that 'No meat, vegetables, or milk not being then healthy, fresh, sound, wholesome, or *safe for human food*, or meat of any animal that has died of disease or accident, shall be brought into the City of New York or held, kept or offered for sale, or sold as such food, or kept or stored, anywhere in said city. . . .' For the purpose of this section, any meat, vegetable, or milk in possession of, or held, kept, or offered for sale by a dealer in food shall, *prima facie*, be deemed to be held, kept and offered for sale as human food."

"During an investigation of food adulterations, an Inspector of the Bureau of Food and Drugs secured a sample of vinegar from a grocery store in the Bronx. Upon analysis it was found that the vinegar in question contained large quantities of arsenic. Upon investigation it was learned that the groceryman had transferred the vinegar from its original container to a second-hand barrel, purchased from a merchant in Brooklyn, who obtained it from a chemical house. The efficient work of the inspectors prevented the sale of this poisonous vinegar from reaching the consuming public."

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## CULTIVATION AND DISTILLATION OF PEPPERMINT IN PIEDMONT.\*

By CONSUL DANA C. SYCKS, TURIN, ITALY.

A small but very profitable industry in Piedmont is the cultivation and distillation of peppermint. The communes which principally yield this crop are Vigone, Pancalieri, Villafranca Piemonte, Polonghera, Lombnasco, Casalgrasso, and Moretta. The crop for 1920 from this district was 100,000 quintals, or 22,000,000 pounds, obtained from 600 hectares or 1483 acres. The crop of 22,000,000

\*Commerce Reports, April, 1921.

pounds after distillation produced 27,000 kilos or 59,525 pounds of peppermint essence valued at 6,000,000 lire.

The demand for Piedmont peppermint greatly exceeds the production, and the local distillers are endeavoring to increase the annual supply by promising higher prices to the cultivators. For the 1920 crop, the distillers paid 30 lire per quintal (220 pounds) for peppermint leaves.

It is stated that the crop for 1921 will be approximately 20 per cent. larger than the 1920 crop, owing to the increased prices offered.

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## REPORT OF THE ONE-HUNDREDTH ANNUAL MEETING AND THE ADJOURNED MEETING OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

The One-Hundredth Annual Meeting of the Philadelphia College of Pharmacy and Science was held in the College Museum on March 28, 1921, at 3:30 P. M., Mr. Howard B. French presiding. There were about 110 members present.

President French read his annual address. The address gave in detail the condition of the property, the number of students in the various classes, the work of the faculty in all the branches of studies, and other matters of vital interest in connection with the management of the building.

The following abstracts from this interesting address call specific attention to certain features of the Centenary Campaign:

"Your President notes with great pleasure the activities of Prof. E. Fullerton Cook, Executive Secretary of your Centennial Committee, and commends the active, earnest and untiring labor which he is giving to the position and also desires to express appreciation of the able assistance which he has received from your office force and from the members of the faculty, as well as for the active co-operation of the Alumni and College membership.

"The sub-committees of your Centennial Committee have been doing remarkable work and deserve all praise and commendation for their activities.

"On February 23rd, in celebration of Founders' Day (February 23, 1821), a large number of people gathered at the College and, although there had been a rather severe snowstorm a few days previous and the streets were not in the best condition, they proceeded to Carpenter's Hall, where a meeting was held at 2:30 o'clock, at

which a large number of descendants of the original incorporators were present. Your President presided, and the minutes of the first three meetings of the College, held in the historical building in February, 1821, were read by your Secretary, Dr. Charles A. Weidemann, after which Mr. George M. Beringer, Chairman of your Board of Trustees, gave a historical address. When the meeting adjourned a motion picture of those leaving the hall was taken by the Stanley News Service, and it is interesting to note that this film has been exhibited in over 200 theatres in Pennsylvania, and also was used by a national service throughout the United States. The College has ordered a copy of the film and will show it during the June celebrations, and will file it in the fire-proof as a historical record.

"At eight o'clock on the evening of February 23rd, a large meeting was held in the Auditorium of your College, at which your President again presided. The meeting was addressed by the Hon. J. Hampton Moore, Mayor of the City of Philadelphia. An interesting address was made by Dean LaWall regarding the 'Founding of the Philadelphia College of Pharmacy and Science.' Prof. H. V. Arny, of the New York College of Pharmacy, delivered an address on 'Pharmacy 100 Years Ago and Today.' Emeritus Professor Samuel T. Sadtler, gave an address on 'The Part That Pharmacists Have Played in the Development of Chemistry.'

"The meeting was full of enthusiasm and adjourned at 11 P. M.

"During the early part of June your Centennial will be celebrated, and from the present until that time the most active co-operation of all interested parties must be given to your Centennial Committee. Much has to be done. Great things have to be accomplished and your executive looks forward to a successful issue as the result of your efforts. He predicts that your College, starting as it does upon the second century of its existence, will have a great and brilliant future, and his hope is that those who will follow will be as actively and zealously interested in the institution and will as loyally support its efforts as those who have been connected with it in the past. To him it has a great future, not only as an educational institution, but as a leader in the science of pharmacy and allied branches, and also in keeping Philadelphia in the forefront as the medical center of this country and even of the world.

"Your President wishes to state that Miss Mary A. Dobbins, as a memorial to her brother, Edwin T. Dobbins, a graduate of your College and a former member of your Board of Trustees, has contributed \$20,000 for the establishment of a library fund, the income from which is to be used for the support of and additions to your library."

The Committee on Nominations then presented its usual report. On motion this report was ordered to be received, entered and filed,

when a motion from the floor necessitated, after due formalities, the reopening of the nominations. Dr. Richard V. Mattison withdrew his name as a candidate for First Vice-President, Dr. Charles A. Weidemann for Secretary, and Mr. G. M. Beringer for Editor of the AMERICAN JOURNAL OF PHARMACY. (Notwithstanding Editor Beringer's withdrawal he was unanimously elected, but later insisted on resigning because of reasons stated in his editorial report.) Additional names were placed before the meeting for a number of the offices, and the election proceeded.

The result of the election is as follows:

President, Otto W. Osterlund.  
 First Vice-President, F. R. Rohrman.  
 Second Vice-President, Joseph L. Lemberger.  
 Treasurer, Aubrey H. Weightman.  
 Corresponding Secretary, Adolph W. Miller, M.D.  
 Recording Secretary, Ambrose Hunsberger.  
 Curator, Heber W. Youngken.  
 Librarian, Freeman P. Stroup.  
 Editor, AMERICAN JOURNAL OF PHARMACY, George M. Beringer.

*Publication Committee.*

Prof. J. W. Sturmer,	Joseph W. England,
John K. Thum,	Prof. Charles H. LaWall,
Prof. E. Fullerton Cook,	George M. Beringer,
Robert P. Fischelis.	

*Committee on Pharmaceutical Meetings.*

Clement B. Lowe, M. D.,	Charles H. LaWall,
George M. Beringer,	John K. Thum,
Heber W. Youngken.	

*Board of Trustees:*

J. M. Baer, Ph. G.,	B. T. Fairchild, Ph. M.,
R. T. Blackwood, Ph. G.,	H. N. Fraser, M. D., Ph. M.,
Milton Campbell, Ph. G.,	Ambrose Hunsberger, Ph. G.,
Theodore Campbell, Ph. G.,	Paul A. Kind,
Wm. L. Cliffe, Ph. M.,	Otto Kraus, Ph. G.,
Jos. W. England, Ph. M.,	R. H. Lackey, Ph. G.,

J. L. Lemberger, Ph. M.,  
 Samuel P. Sadtler, Ph. D.,  
     LL. D., Chairman,  
 A. W. Miller, Ph. G., M. D.,  
 H. K. Mulford, Ph. G.,  
 O. W. Osterlund, Ph. D.,  
 J. C. Peacock, Ph. G.,  
 W. H. Poley, Ph. G.,

W. D. Robinson, Ph. G., M. D.,  
 F. R. Rohrman, Ph. G.,  
 S. P. Sadtler, Ph. D., LL. D.,  
 R. S. Sherwin, Ph. G.,  
 R. M. Shoemaker, Ph. G.,  
 F. P. Streeper, Ph. G.,  
 S. P. Wetherill,  
 Jos. W. England, Ph. M.,  
     Vice-Chairman.

After the tellers had concluded their report, Dr. Robinson moved that a committee be appointed to escort the newly elected President to the platform. President French appointed Dr. Robinson to this duty, and then congratulated Mr. Osterlund upon his election and expressed his good wishes for a successful administration.

Mr. Peacock moved that a vote of thanks be tendered Mr. French for the impartial manner in which he had presided. This motion was carried.

Mr. Osterlund then replied to Mr. French's congratulations.

President Osterlund then took the chair.

Mr. Peacock moved that the thanks of the College be tendered to Mr. French, Dr. Mattison and Dr. Weidemann for their valued services over a long period of time. The motion was adopted by a rising vote.

Dr. Robinson then moved (and was seconded) that a committee of five be appointed to draft resolutions expressive of the valuable services rendered the College by Messrs. French, Mattison and Weidemann.

The meeting then adjourned with announcement of a resumed meeting which took place on April 4, 1921, at 3:00 P. M.

The adjourned meeting was called to order by President Osterlund. Minutes of the previous meeting were read by Secretary Hunsberger. Prof. LaWall read a report for the Publication Committee, and the annual report of the Editor. The first report conveyed the sincere regrets of the members in regard to the resignation of Editor George M. Beringer, whose conduct of the policies of the JOURNAL left nothing to be desired. It recommended that the College appropriate the usual amount for the use of the AMERICAN JOURNAL OF PHARMACY for the ensuing year, and also that Mr. Ivor Griffith be selected as the new Editor of the JOURNAL.

Prof. Stroup moved that this report be received and that the recommendations be adopted. The motion was seconded and carried.

The retiring Editor, Mr. George M. Beringer, reported that the JOURNAL had progressed in many ways. The following is a brief statement of the progress of the JOURNAL since 1917:

Increase in mailing list .....	165	per cent.
Increase in total revenue .....	188	" "
Increase in publication expense .....	112	" "

The report further stated that Volume No. 92 of the JOURNAL had been completed and that it contains 946 pages of reading matter, the index requiring sixteen additional pages. The wide range of topics that have been considered in the twelve monthly issues of the JOURNAL is well reflected in the scope of the index. Sixty-three original papers prepared by forty-six authors were published in this volume, and the support that the JOURNAL has received through these contributions from eminent pharmacists and scientists is very gratifying.

The conclusion of the report expresses Mr. Beringer's desire to be relieved of the editorship because of the extent of his burdens and the demands of his personal business, which has made it unusually difficult for him to dedicate to the JOURNAL the time required to carry on the editorial work along the lines designed to hold up the JOURNAL as a potent factor in the pharmaceutical field.

Mr. Peacock moved that the Editor's report be received and filed and that certain recommendations be referred to the Committee on Publication with power to act, and that the other recommendations therein be considered as new business.

Mr. Fischelis moved that a special vote of thanks be extended to Mr. Beringer for the great services he has rendered the College as Editor. Mr. Cliffe seconded this motion, and it was further decided that a resolution of thanks be prepared and entered upon the minutes.

A favorable report of progress was given by the Curator, Prof. Youngken, noting particularly that a number of medicinal plants already mounted had been presented to the Museum. These had been properly filed in the Herbarium. Specific mention is made of interesting specimens by Prof. LaWall, Mr. Beringer and Prof.

Moerk. Dr. John Small has presented to the College an old-fashioned bronze mortar.

It was moved and seconded that this report be received.

Mr. Jos. W. England, Chairman of the Committee on By-laws, presented a recommendation for revision of the by-laws, which would make all persons engaged in applied science eligible for membership.

The President, Mr. Osterlund, appointed the following committee to consider certain changes in the by-laws regarding active and associate membership in the College:

Joseph W. England, Chairman;  
Dr. C. A. Weidemann,  
Warren H. Poley,  
Josiah C. Peacock,  
Edward T. Hahn.

With deep regrets it was moved that Mr. Beringer's declination as Editor of the *AMERICAN JOURNAL OF PHARMACY* be accepted.

Prof. LaWall specifically moved that Mr. Ivor Griffith be nominated Editor. Mr. Peacock seconded the motion. The Secretary cast the ballot for Mr. Griffith, and he was unanimously elected.

The Committee on Necrology reported the death of eleven active members and two associate members during the year 1920.

Prof. Freeman P. Stroup, Librarian, verbally reported that the library had been used extensively during the past year.

Prof. Cook read the report of the Committee on Centennial Celebration.

President Osterlund explained that Prof. Cook was working night and day with other members of the faculty and College in order to make the campaign a success.

The President appointed the following Committee on Resolutions to retiring officers:

Joseph W. England, Chairman;  
William Duffield Robinson,  
Robert P. Fischelis,  
Josiah C. Peacock,  
Charles H. LaWall.

The meeting was adjourned to meet the call of the chair.



## SCIENTIFIC AND TECHNICAL ABSTRACTS

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COLOR TEST FOR OXALIC ACID.—A few crystals of resorcinol are added to about 5 mls (Cc.) of the unknown solution in a test-tube, and the mixture is warmed slightly to dissolve the resorcinol. It is then cooled and 5 mls (Cc.) of concentrated sulphuric acid are carefully and slowly poured in along the side of the tube so as to form a layer. A blue ring will be formed at the junction of the two layers, if oxalic acid is present. The color is best seen if held to the light in front of a sheet of white paper. Care must be taken that the mixture does not warm up appreciably. If the blue color does not appear in a few minutes, the mixture is shaken thoroughly, and after cooling somewhat 5 mls (Cc.) more of sulphuric acid are added. Should the color still fail to appear, the mixed contents of the tube should be gently warmed over a flame (not boiled) when an indigo blue color will diffuse throughout the liquid. If the mixture be cooled with ice-water, the color will disappear only to reappear again on heating. If the mixture be boiled a few minutes, the color will turn a deep dark *green*, which will become a light yellow-green on cooling. If to the cold yellow-green solution an equal volume of sulphuric acid be added so as to form two layers, the *blue* color will again appear. It is believed that all these reactions taken together are characteristic of oxalic acid alone.

This test may be made sensitive to one milligramme if the dry unknown substance be warmed with two drops of a 10 per cent. aqueous resorcinol solution and the sulphuric acid added drop by drop. The blue color then appears immediately. For very dilute solutions of oxalic acid or its salts, it is best to evaporate to a concentration of about 10 per cent.

If interfering substances are present the oxalic acid may be precipitated in ammoniacal solution as the calcium salt, washed with water, and the test applied directly to an aqueous suspension of the salt.—(*Journal of the American Chemical Society*, through *Merck's Report*, April, 1921.)

CLOVE OIL FROM CLOVE STEMS.—The first number of a new journal *The Journal of Indian Industries and Labour*, which is published in Calcutta, contains an article by S. T. Gadre, industrial chemist to the Government of the United Provinces, Cawnpore, giving the results of study of the yield of oil from clove stems, that is, the portions of the branches just adjoining the clove proper. Some interesting data concerning clove production are also included. The principal source of the spice is from forests in the islands of Zanzibar and Pemba, in which a total of nearly five million trees are found, covering over 50,000 acres. Some of the trees are ninety years old. The production 1918-1919, a banner year, was about 29,000,000 pounds. The stems contain a brown substance, which is used as dye by the natives, but the bulk of the stem material was formerly exported to Germany, where it was distilled, and the oil brought into the markets in which the oil from the clove itself was sold. The exhausted stems were much used as an adulterant for cloves. Gadre obtained a large consignment of the stems and subjected them to distillation. He found that the oil corroded a copper still, and had to use a tinned one. He found a yield of about 4.5 per cent. The oil is pale yellow, deepening by exposure to light and air, and turning brown when heated in the water bath. It has an irritating action on mucous membranes. It conforms to all the requirements of the B. P. and U. S. P. The total eugenol by Umney's test was 93.09 per cent. The free eugenol by the method of Varley and Bolsing—said to give results within 0.5 per cent.—was 69.86 per cent.

Clove oil has several important uses. Its value as a source of synthetic vanillin is well known. It was found to have a germicidal value in treating some diseases of camels during the war. The price advanced greatly during that time, but has now fallen somewhat. Gadre thinks that the distillation of the stems can be made a profitable enterprise—H. L.

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PROTEIN IN FOOD AS A CAUSE OF HEADACHE.—The proteins of food are capable of producing headache in individuals whose protein mechanism is inadequate for those particular proteins. The articles which are found most often to occasion disturbances, headache, and other manifestations are, in the order of their importance, meat extractives, fruit and fruit extractives, eggs, meat, coffee, tea, choco-

late, cocoa, and certain vegetables, such as tomatoes, mushrooms, rhubarb, and cucumber. Any protein may be the cause. In one case, the protein of oats, and also of potato, caused headache. The protein extracts such as meat soups and fruit juices are even more potent than meat or fruit. This shows that the harmful protein is soluble. The author considers that the usual American hospital diet of meat, soup, eggs, and fruit juice is bad, not only for cases of protein poisoning, but also for infectious diseases, since it has a tendency to reduce the normal alkali reserve which is needed to combat infection. Migraine and periodic headache are primarily due to inherited deficient metabolism, and can, in every instance, be cured by a properly restricted diet.—Dr. R. C. Brown, *Wisconsin Med. J.*, 1920, 19, 337; *J. Amer. Med. Assoc.*, 1921, 76, 338.

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IMPROVED INFUSION OF DIGITALIS.—The following *modus operandi* gives an infusion which represents the full therapeutic activity of the drug, such as is not attained by the method official in the U. S. P. ix. One part of digitalis leaf, in No. 60 powder, is treated with 100 parts of boiling water, and kept for one hour on a boiling water bath, with frequent stirring. It is then filtered, and may be kept in completely filled corked bottles sealed with hard paraffin. Specimens thus prepared and stored in February, 1918, have retained their therapeutic activity unimpaired to date, as shown by the cat test. Since the official U. S. P. infusion does not represent the drug, the standardization of the leaf does not ensure the uniform activity of the official infusion. The infusion prepared by the method described above has not that defect. It is fully active. The dose is exactly ten times that of the U. S. P. 1:10 tincture. It is shown that the residual marc of this infusion is quite inactive, and, therefore, completely exhausted. It was found that the drug is completely exhausted in the percolation process of the U. S. P. tincture. Therapeutically, there is nothing to choose between this tincture and the equivalent dose of the infusion prepared as directed. The results obtained are identical. There is no experimental evidence to support the view that a necessary qualitative difference exists between the action of the tincture and the infusion of digitalis, when the latter is prepared properly.—S. Weiss and R. A. Hatcher, *J. Amer. Med. Assoc.*, 1921, 76, 508.

CHINESE PEANUT OIL.—The extraction of Chinese peanut oil from *Arachis hypogaea* is a profitable industry of the province of Kwantung. The peanuts are first washed free of soil and dried in the sun. The nuts are then passed through a large mill, similar to that used for husking rice, and the mixture of whole nuts, husks and kernels are sieved over coarse rattan sieves. The refuse is used for fuel. The husked nuts are now taken to the pressing shed, and are pounded by a very heavy stone pestle in a narrow mortar by hand and foot pressure. The peanut meal is transferred to a shallow wooden tub, which is inverted over a cauldron of boiling water and thoroughly steamed to render the meal more adhesive. The steaming meal is removed in mould form from the tub and is then made into cakes by means of rattan rings, of which ten or so are used to form a cylinder of about 12 inches in diameter. A sufficient number of rings being prepared, the pressing is the next operation. The press consists of a huge hollowed-out tree trunk 18 or 20 feet in length, and about 2 feet in diameter. The trunk is cleaned out except at opposite ends to a diameter of about 12 or 14 inches. A slit along the upper surface of the log allows the contents to be seen. The slit at one end of the log is expanded into a wide open gulley, in which the cakes of meal and some wooden wedges can be inserted. The floor of the trough has a slope, and at the lowest end there is a hole for the drainage of the expressed oil. The press is then filled with the cakes up to the gulley or open portion. Against the outer end of the cakes are placed circular wooden blocks, and behind these are three rows of brick-shaped blocks. Into each row of the latter is forced a wedge by means of a huge wooden mallet. By this means enormous pressure is exerted, and as the brick-shaped blocks slacken, others are put in, until the press is tightly packed. It is then left for twenty-four hours for the oil to trickle out into a large pan under the hole in the trunk. All the oil not being removed by the first pressing, the pressed cake is split into thin plates, which are fried for a few minutes and again submitted to pressure, which yields extra oil. The oil thus expressed is ready for sale, and the residual meal finds a ready market as manure.—Abstracted from the *Hongkong Weekly Press*, December 4, 1920; through the *Pharm. Journ. and Pharm.*, April, 1921.

TRYPANOCIDAL ACTION OF ARSENIC AND ANTIMONY COMPOUNDS.—Quantitative studies by Carl Voegtlin, Homer W. Smith, and others, into the power of certain drugs to sterilize an infected animal are the subject of the recent report to the U. S. Public Health Service. Specifically, the studies were directed to ascertaining the minimum dose, injected intravenously, of certain compounds of arsenic and antimony (important in the treatment of relapsing fever, syphilis, sleeping sickness, etc.), which would prove lethal to the majority of white rats that had been infected with trypanosoma, and also the minimum dose that would prove effective in destroying the parasites.

The minimum effective dose, below which the drug failed to destroy the parasites, was found to be fixed partly by the reaction between the drugs and the parasites, and partly by the rate at which the drug was absorbed by the tissues of the host. Thus, sub-effective doses antimonyl lactate ceased to act, not when they had killed a certain number of parasites, but when absorption by the host had lowered their concentration below their "threshold."

Differences in the effectiveness of different arseno and pentavalent compounds are held to depend on the ease with which they are oxidized or reduced in the body, oxidation or reduction being necessary before they can exert their chief toxic action.

The authors hold that, although the results obtained do not indicate with absolute accuracy the clinical value of a compound, they do furnish a valuable quantitative comparison with other compounds.

UTILITY OF ANTIPLAGUE VACCINES.—That the utility of vaccines and serums in antiplague work is at the best not proved is asserted by G. W. McCoy and C. W. Chapin in a recent report of the U. S. Public Health Service. Antiplague vaccine was first used on man in 1897 by Haffkins, who used old killed broth cultures in large doses and claimed that marked reduction in the attacks of the disease resulted. Other observers report much less brilliant results, possibly as later work suggests, because different strains of the plague organism affect the efficiency of the vaccine. Innoculation by living virulent cultures has been found promising by other workers, but its value has not been demonstrated. Vaccination is not known to have ever controlled a plague outbreak.

Evidence in regard to the prophylactic value of serum is meager. Certainly it confers no complete or durable immunity. As a therapeutic agent, however, serum seems to have had some success.

The authors regret that popular and professional interest should so often center on vaccines and serums where anti-rat measures are demanded. If people want to be vaccinated for plague, let them; but the important thing is to kill the rats.

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TOXIC EFFECTS OF SHAKING ARSPHENAMINE SOLUTION.—That the shaking of alkalized aqueous solutions of arspenamine in the air for 60 or even 30 seconds greatly increases their toxicity, probably by oxidation, is stated by G. B. Roth as a result of experiments described by him in a recent report to the U. S. Public Health Service.

Some preparations, of neoarsphenamine particularly, may be difficultly soluble, and such are liable to be shaken to hasten solution. The results from this are almost always highly toxic and should not be used clinically; although a relatively low-grade preparation may tolerate 5 or 10 seconds of shaking and yet pass the Hygiene Laboratory tests. Shaking in a closed bottle containing no air seems not to increase the toxicity.

The author concludes that the toxicity of the solutions is greatly influenced by the manner of their preparation, and that they should not be made in an open mortar or a large beaker.

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FRACTIONATION OF CHAULMOOGRA OIL.—An article by A. L. Dean and Richard Wrenshall, just reprinted by the U. S. Public Health Service from the *Journal of the American Chemical Society*, describes experiments made at the University of Hawaii into the fractionation of chaulmoogra oil. The hope was to find a fraction that contained the curative principle without including the one that renders the whole oil intolerant to many patients.

Four lines of experimental study were followed: (1)\* Separation of the fatty acids by crystallization from alcohol was tried and abandoned because the fractions gave low melting solids and oily mother liquids. (2) Separation by means of barium acetate was abandoned as unsuitable to production on a large scale. (3) Frac-

tional distillation of ethyl esters under high pressure, though considered promising, was abandoned in favor of (4) direct fractional distillation.

By the last method four esters of the fatty acids of the oil were developed and were used on four groups of patients, a considerable number of whom become clinically and bacteriologically free from leprosy. But it was impossible to identify this effect with anyone of the esters.

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DETERMINATION OF LACTOSE IN MILK BY COLORIMETRIC METHOD.—The method is a simple adaption of Folin's latest blood sugar determination to the estimation of lactose.

Method: To 1 c. c. of milk in a 100 c. c. flask add 2 c. c. of 10 per cent. sodium tungstate solution and 2 c. c. two-thirds normal sulphuric acid, the latter drop by drop. Mix and let stand five minutes; dilute to 100 c. c. and filter. Place 1 c. c. of filtrate and 1 c. c. of water in a Folin sugar tube; to the second sugar tube add 2 c. c. of standard lactose solution A. And to a third tube add 2 c. c. of standard lactose solution B. To each of the three tubes add 2 c. c. of alkaline copper solution and boil for six minutes. Cool in water, add 2 c. c. of Folin molybdate phosphate solution and let stand a few minutes. Standard A contains 0.5 mg. lactose per 2 c. c. Standard B contains 0.7 mg. per 2 c. c. The reading of the standard divided by reading of unknown, multiplied by 5 if Standard I is used, or 7 if Standard II is used gives the grams of lactose per 100 c. c. of milk.

To make the Standard lactose solution make an accurate 1 per cent. lactose solution in distilled water. Preserve with toluol. For Standard I dilute 12.5 c. c. of the stock solution to 500 c. c. For Standard II dilute 17.5 c. c. of stock solution to 500 c. c.—R. G. Owen and Roth Gregg, *J. Lab. & Clin. Med.*, Jan., 1921.

## MEDICAL AND PHARMACEUTICAL NOTES

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TOXIC IDIOPATHY.—In a lecture at the Royal Institution on March 11, Dr. John Freeman, St. Mary's Hospital, London, gave a most interesting account of the results of recent research on the idiosyncrasy of the human subject with reference to various animal and vegetable substances introduced into or generated in the living body as food, or in other forms. As an illustration of popular belief in such idiosyncrasy he quoted a specimen of ballroom "conversation" from *Punch* of the 'sixties of the last century: "He: 'D'ye know, my grandfather couldn't bear to have a cat in the room.' She: 'Really! How strange! and my Aunt Dorothy always fainted when she smelled a rose.'" This popular notion, which hitherto had been generally pooh-poohed as a superstition, had now been verified by scientific investigation. It had been ascertained that, in addition to the well-known case of hay-fever sensitive, upon whom grass pollen, and particularly Timothy grass pollen, which in this country was more abundant and widely dispersed than that of any other species, set up the inflammatory conditions of the mucous membrane, and in severe cases the constitutional disturbance characteristic of the malady, many other plant and animal substances had a selective action upon certain individuals, and it was also proved that this idiosyncrasy ran in families. Thus, there were cat-sensitives, who were made ill or contracted asthma by breathing in fragments of a cat's hairs or its shed skin scales, or dust from its secretions; and there were also horse-sensitives, who suffered similarly, even by indirect contact with horses, or by eating horseflesh. In one instance cited by the lecturer, a little girl ate some sausages purporting to be made of ox-beef, but she swooned after taking the sausages, and on subsequent inquiry it was found that horseflesh had been used in their composition. A large number of cases were described of intolerance of certain foods. Thus, one man's poison was carrots; another's cabbage; and so on, and the explanation of the incompatibility of cows' milk with some babies was to be found in idiosyncrasy. If another animal's milk were used, or the cows' milk were denatured, a eupeptic condition could be established. In all these cases it was possible to apply a simple diagnostic test which discriminated between feigned and gen-



nine idiosyncrasy. In hay-fever the conjunctiva becomes bloodshot, and the introduction in some form of the suspected substance into the eye always produces this bloodshot effect. But as it is seldom convenient to apply this test, the urticaria effect is more generally used. This consists in the application to the skin of the arm, from which, by slight scratching, the epidermis has been partially removed, of the suspected substance, or of its precipitated proteids. If there is a reaction in the form of an urticarial eruption, the person is sensitive to the substance, which is therefore contra-indicated as an article of diet, or as a pathogenic vegetable, or animal substance. The lecturer quoted a number of cases from his own hospital and private practice, in which bronchial-asthma in cat and other sensitives had been cured by the elimination of the peccant organic substance. He confessed that the mechanism of these phenomena was still unexplained, but was hopeful that future research would reveal the rationale of it. A few weeks before his death, Lord Moulton, to whom the lecturer had described some of his work on toxic idiopathy, had exclaimed, "At last Nature has come out into the open and we shall catch her."—From the *Pharmaceutical Journal*, March, 1921.

**QUININE ACETOSALICYLSULPHATE.**—The solubility of quinine sulphate in water at ordinary temperature is usually stated as about 1 part in 800, and that of acetyl-salicylic acid as 1 in 400 of water. On adding the two compounds to water, in ordinary dosage quantities and stirring, it is obvious that the mixture is much more soluble than either of the constituents. It was fairly certain that an acid salt is formed, and it seemed worth while to determine which proportion of acid gave the maximum solubility. By adding the acid in increased molecular proportions, it was found that the best result was obtained by 4 molecules of acetylsalicylic acid to 1 of quinine sulphate. That a definite compound is formed is evident from the behaviour of solutions on evaporating, no appearance of separate constituents being visible. Taking B as representing  $C_{20}H_{24}N_2O_2$ , we may give the formula of the salt as:



It is quite usual to give the formula of a salt with the maximum water of hydration which it is capable of taking up. In the case of the salt in question that seems to be 9 molecules, but it readily dries or effloresces to the proportion of 4 molecules, so that the formula

given is probably the more convenient expression. The salt is soluble in water to the extent of 1 part in 50. After drying in desiccator for some hours the salt melts at  $96^{\circ}$ , much below the m.p. of either of its constituents.—D. B. DOTT, *Pharm. Journal and Pharmacist*, March, 1921.

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THEOBROMINE AND CAFFEINE; REACTION TO DISTINGUISH.—The difference between the behaviour of theobromine bismuthic iodide and the corresponding compound of caffeine towards the reducing action of hydriodic acid may be used to differentiate these two substances. The test is conveniently performed as follows:—0.05 g. of theobromine or caffeine is shaken with 10 c. c. of water and 0.5 c. c. of freshly prepared potassium bismuthic iodide solution. In each case an orange-coloured precipitate is formed, and 5 drops of a 10 per cent. tincture of iodine (not freshly prepared, so that it may contain a small proportion of hydriodic acid) is added. The colour of the caffeine bismuthic iodide precipitate changes to a bright red, whilst the theobromine precipitate becomes brown in 15 mins., and dark chocolate brown in less than 30 mins.; owing to reduction. A dilute solution of hydriodic acid, containing not more than 1 per cent. of hydrogen iodide, may be used instead of the tincture of iodine.—M. MALMY, through *Journ. of the Society of Chemical Industry*, March, 1921.

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A NEW COMPOUND OF BARBITURIC ACID.—At a recent meeting of the *Société de thérapeutique*, Paris, a new compound of barbituric acid was described by Daniel Bardet (*L'Union pharm.*, Jan., 1921, p. 1). This is diethyl-diallyl-barbiturate of diethylamine, and is a combination of diethyl-barbituric acid (veronal) and diallyl-barbituric acid (dial) with diethylamine. This compound is soluble in water 1:3, this solution containing 10 per cent. of veronal and 10 per cent. of dial. Such a concentrated solution is easily injectable subcutaneously or intravenously, and is accordingly very convenient of administration and rapid in its effects. Daniel states that this new compound is non-toxic in ordinary effective doses; its action is on the central nervous system; it can be employed as an anæsthetic in operations not requiring complete muscular relaxation; it is a valuable adjunct to general anæsthesia, suppressing the period of excitation and allowing of the employment of a minimum quantity of anæsthetic; it has the drawback of not always giving the same results in the same

doses; its slow elimination prolongs its hypnotic action too much and tends to mask postoperative effects, and this second drawback serves to contra-indicate its use in large doses and in abdominal operations. Its great advantage is its solubility, and in spite of its drawbacks there are fields for its employment that may bring it into use in medicine and surgery.—*The Prescriber*, April, 1921.

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## NEWS ITEMS AND PERSONAL NOTES

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ESTABLISHMENT OF A FOOD RESEARCH INSTITUTE.—The Carnegie Corporation of New York has entered into an agreement with Leland Stanford, Jr., University, by which a food research institute is to be established at the university for the intensive study of the problems of production, distribution and consumption of food. The corporation expressed hope that the new organization will in time be known as the Hoover Institute. The corporation will provide \$700,000 for its support for ten years. Dr. C. L. Alsberg, Chief of the Bureau of Chemistry of the U. S. Department of Agriculture, has been elected the first director.

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THE EXAMINATION FOR FAIRCHILD SCHOLARSHIP.—Candidates will be examined in the Schools and Colleges of Pharmacy, members of the American Conference of Pharmaceutical Faculties, June 11, 1921. The Deans of the respective institutions will have supervision over the examinations.

The following recommendation was unanimously adopted at the New York A. Ph. A. meeting by the Section on Education and Legislation A. Ph. A., the American Conference of Pharmaceutical Faculties and the National Association of Boards of Pharmacy, in joint session, and this will serve as the basis for award:

The Fairchild Scholarship is to be awarded by a competitive examination to candidates who are High School graduates, and who have completed their first year work in a School or College of Pharmacy, member of the American Conference of Pharmaceutical Faculties, and each School or College shall be limited to two candidates.

One award is made each year.

IMMIGRANT HEALTH AND THE COMMUNITY.—The Carnegie Corporation of New York has recently made public the following extract from a forthcoming book on "Immigrant Health and the Community," which is to present the fifth of the Americanization studies made under the auspices of the Corporation:

"The local drug store, the place where most patent medicines are purchased, is an important center of medical advice. There are several reasons for this.

"Usually the local druggist or someone in his employ speaks the immigrant's language, and if there is a large colony of any one mother-tongue group there are certain to be several drug stores where the language is spoken. The drug store is localized and therefore readily becomes known to the immigrant.

"We must appreciate also that the pharmacist is properly regarded by many immigrants as a man of learning. The drug store is anxious to co-operate with the immigrant and the immigrant's local organizations.

"Drug stores are important from the medical standpoint, because it is to them rather than to the doctor that the immigrant first turns. New arrivals and people who have not had occasion to use a doctor since their arrival frequently turn to the druggist for advice about doctors. Local doctors are, therefore, the friends of the druggist, and his store is a meeting place both for social and professional acquaintances who chat, and for business competitors who keep an eye on one another."

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## BOOK REVIEWS

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"LABORATORY MANUAL FOR THE DETECTION OF POISONS AND POWERFUL DRUGS." By DR. WILHELM AUTENRIETH, Professor in the University of Freiburg, i. B. Authorized translation by William H. Warren, Ph. D. Fifth American edition. P. Blakiston's Son & Company, Philadelphia. 342 pages; \$3.50 net.

In the preface, the translator states that this "present English edition is a translation of the fourth completely revised German edition, as a fifth German edition, so far as the writer is aware, has not yet appeared."

It is also stated that "owing to the prominence attained of late by wood (methyl) alcohol, due to ignorant or criminally careless

substitution of this intoxicant for grain (ethyl) alcohol, this substance has been added to the list of volatile poisons. Aside from minor corrections of the text, the omission and correction of certain tests, the introduction of a few new tests of recent appearance in the literature, and the expansion of the index to include authors as well as subjects, no changes of importance have been made in the last edition of this work."

Laboratory workers and students in toxicological chemistry will do well to include this book in their "five-foot shelf." Being quite comprehensive, it will be found generally useful, whether for experimental practice or for guidance in isolating and estimating poisons in cadaveric material, food, etc.

The scheme of analysis divides poisons into three groups, which are dealt with in the first three chapters. Group I includes those substances which, when heated, volatilize without decomposition and distil with steam from an acid solution. The members of Group II are non-volatile organic substances, which do not distil with steam from an acid solution, but which may be separated from extraneous matter by extracting with hot alcohol containing tartaric acid. Group III includes all metallic poisons. A few poisons such as mineral acids, caustic alkalies, oxalic acid and potassium chlorate are tested for by separate tests, owing to inherent peculiarities of these substances. Chapter IV embraces this group. Chapter V is devoted to special qualitative and quantitative methods for arsenic, alkaloids and salicylic acid. The quantitative estimation of alkaloids and other active principals in raw materials and preparations according to the German Pharmacopœia, is taken up in Chapter VI. Chapter VII deals with the detection of carbon monoxide blood, blood stains and human blood.

In the appendix are given formulæ for the preparation of general alkaloidal reagents and the other reagents and solutions used.

In short, the treatment of this subject is quite thorough and systematic, with liberal explanatory notes and many references to original articles. The book commends itself to those interested in toxicological and alkaloidal work.

R. R. F.

YEAR-BOOK OF PHARMACY. Published by J. and A. Churchill. London, 1920; 594 pages.

This is an annual British publication containing abstract of papers contributed to scientific journals, together with the transactions of the British Pharmaceutical Conference held in Liverpool in July of 1920.

The first 347 pages of this book are devoted to the abstracts relating to pharmacy, materia medica and chemistry of drugs. These were selected from contributions to scientific journals during the period from July 1, 1919, to June 30, 1920. While the great majority of the abstracts are taken from European periodicals, quite a large number of them are found to be of American origin.

The plan of the book is unique. The abstracts dealing with chemistry are arranged first and these are divided into convenient sub-sections. This is followed by the sections on materia medica and pharmacy, each being divided into sub-groups according to the nature of the abstract.

Then follows an interesting and useful research list covering several pages. It is probable that some of the suggestions found here have already been taken up for investigation.

The remainder of the book contains the transactions of the British Pharmaceutical Conference of 1920. In the scientific section of this part are found many communications and discussions which directly concern the pharmacist and the pharmaceutical chemist. At the close of these transactions is found a list of the members of the conference.

The book is thoroughly indexed and represents, in condensed form, practically all the year's work accomplished in pharmacy and its allied sciences. It certainly merits recommendation to the American as well as the British pharmacist and analyst as an excellent book for reference.

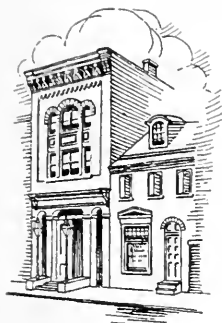
E. J. H.

# THE AMERICAN JOURNAL OF PHARMACY

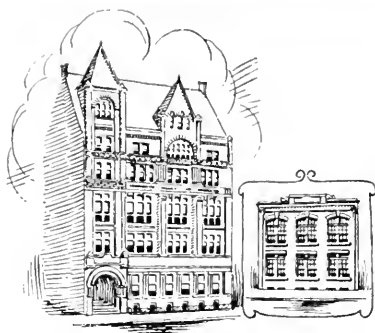
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No. 6



YESTERDAY.



TODAY.

## A MESSAGE FROM THE NEW PRESIDENT OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

In assuming the duties of President of the College of Pharmacy and Science of Philadelphia, I do so with a full realization of the responsibility involved; also that it is a transitional period in the affairs of the institution, which makes it a peculiarly critical and important period if the College is to maintain and carry on the splendid record of the years gone by. No one person can make success, but I am counting on the undivided and loyal co-operation of every member of the College and I shall do everything I can at once to put the institution in shape for active, progressive effort.

*William O. Braisted.*



TOMORROW.

## WILLIAM C. BRAISTED, M. D.

*President of the Philadelphia College of Pharmacy and Science.*

To lead the College into the second century of growth and service the members have chosen as its President, Rear Admiral William Clarence Braisted, former Surgeon General of the United States Navy, President of the American Medical Association, and Chairman of the National Board of Medical Examiners.

Throughout the World War and the period of demobilization Admiral Braisted had command of the Navy's Bureau of Medicine and Surgery, and his conspicuous services gained for him an international reputation for broad vision and efficient administration. Secretary Daniels' Report of the Navy's activities in the War is in reality a tribute to the services of Admiral Braisted. That report says:

"Recognition of the excellence of the work of the Medical Department of the Navy, under the direction of Surgeon General Braisted, has come from medical authorities at home and abroad. At the last session of the American Medical Association Admiral Braisted was elected its President, the highest honor that can come to an American physician. This was not only a tribute to the Surgeon General, but a tribute as well to the Naval medical force. It is gratifying also to know that he has been made an Honorary Fellow of the Royal College of Surgeons of Edinburgh, one of the few Americans upon whom this honor has been conferred."

Admiral Braisted was born in Toledo, Ohio, on October 9, 1864. In 1883 he was graduated a Bachelor of Philosophy from the University of Michigan. Three years later, when he was graduated a Doctor of Medicine from Columbia University, he was an honor man in his class. After two and a half years of service in Bellevue Hospital in New York he practiced medicine in Detroit until, in September, 1890, he entered the Navy as Assistant Surgeon.

Step by step William C. Braisted advanced in the service, serving on many vessels and at many naval hospitals. Twice he was instructor in surgery in the Naval Medical School. For zeal and skill in caring for the wounded after the battle of Puerto Cabello he was decorated with the Order of Bolivar by the President of Venezuela. In 1904, he fitted out and equipped the hospital ship "Relief."

During the Russo-Japanese War he represented the Medical De-



partment in Japan and was decorated by the Mikado. As Assistant Chief of the Bureau he assisted in the complete reorganization of the medical service of the Navy. For a time he served as Attending Physician at the White House in the administration of President Roosevelt.

From 1912 to 1914, he was Fleet Surgeon of the Atlantic Fleet. In 1913, he was elected President of the Association of Military Surgeons of the United States. February 18, 1914 he was appointed to the post of Surgeon General and Chief of the Bureau of Medicine and Surgery, with the rank of Rear Admiral.

Upon the shoulders of Admiral Braisted fell the responsibility for the surgical, medical and pharmaceutical readiness of the Navy in the World War, not only in the matter of supplies, but in personnel also. So well did he perform his task that every call made upon the bureau was answered. To his care nearly 120,000 sick and wounded soldiers, sailors and marines were entrusted; his jurisdiction extended over the Marine units fighting in France, over the Naval aviation stations, over health conditions in submarines and the Sanitary and Medical features of the transportation of the Army to Europe accomplished by the Navy in fact, over the myriad activities touched upon by the Naval forces.

An idea of the magnitude of his task may be obtained from the fact that of 1,235,933 American troops returned by June 20, 1919, 111,522 of them were sick or wounded and in his keeping.

Admiral Braisted has brought about the reorganization and enlargement of the Medical and Hospital Corps by securing necessary legislation for increased personnel with increased rank and pay. He has secured hospital construction and administration of the most up-to-date kind of the Navy. He has founded four colleges at Newport, Norfolk, the Great Lakes Training Station and San Francisco, respectively, for the training of Naval pharmacists. In addition he established a correspondence course in pharmacy for men in the Navy's Hospital Corps. The first hospital ship of the Navy to be designed and fitted out from the keel up for the special purposes of the Medical Department, now under way at the Navy Yard at Philadelphia, was undertaken under his auspices. He has had prepared the book of instructions for the Hospital Corps, as well as the Manual of the Medical Department for Medical Officers, the Compend for Masters of Auxiliary Vessels, special reports on the War in Europe, etc.

Recognition of the distinguished services of Admiral Braisted has not been lacking. Among the honors accorded him are the degree of Doctor of Laws by the University of Michigan and Jefferson Medical College, and the degree of Doctor of Science by Northwestern University. He is President of the Board of Visitors of the Government Hospital for the Insane, a member of the Board of Regents of the American College of Surgeons, a Director of Columbia Hospital in Washington, and once Vice-Chairman of the War Relief Board of the American Red Cross. During the war he was a member of the Central and Executive Committee of that body.

He is President of the National Board of Medical Examiners and a member of the American Medical Association, the Southern Medical Association, the American Academy of Medicine, and many other societies. Dr. Braisted is also Chairman of the Provisional Board of the Gorgas Memorial Institute begun recently at Panama, a great institution for research into tropical diseases and preventive medicine for the welfare of the entire world.

For his services during the war he was awarded the Distinguished Service Medal of the Navy.

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## EDITORIAL

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### LOOKING FORWARD.

It is not the mystic number one hundred, or the recent centennial celebration, but the necessity for adjustment to present-day conditions, that has brought about the expansion of the Philadelphia College of Pharmacy and Science. The marvelous progress of science—the advent of labor-saving machinery, to which is due the development of large pharmaceutical manufacturing establishments—the advances in medicine, particularly in diagnosis, calling for trained bacteriologists and clinical chemists—all these have trended toward specialization by students in pharmacy, and opened new fields of service for the institution.

To be sure, the founders established a college of apothecaries. But the old-time apothecary is no more. He has gone the way of the tallow candle, and the Franklin stove. His place has been taken by the modern prescriptionist, and the manufacturer of medicinal

products, the assayist and control chemist, the bacteriologist, the clinical chemist and hospital technician, the distributor of sick-room appliances, the manager of the modern drug emporium, and the merchant prince dealing in drugs on an extensive scale.

So there have been added from time to time courses of training for these specialists; and the founders would be astonished as much by the present-day diversity of functions of their College, as they would be by the present-day appearance of their beloved Philadelphia, with its tall buildings, its trolley cars, automobiles, telephones, and electric light.

There comes now the necessity not only for more specialization, but for courses in the basic sciences, so that our students may have the advantages of a broader and stronger foundation upon which to rear the superstructure of special training. This will bring to them greater possibilities in pharmaceutical research, for it will provide new methods of attack in the solving of research problems.

To supply these basic courses, the College must have added facilities, which can be provided only in new and larger buildings, specially planned to meet our needs. Such buildings call for an appropriate setting, and a proper environment. Hence the plan of new buildings on the Parkway, or in the suburban districts.

But buildings fill only material needs; and there are in prospect accessions to the faculty—men who will administer the courses in the languages, in mathematics, in physics, and in physical chemistry, and make possible plans of study which conform to the best academic standards, and at the same time provide training for a specific line of activity in some pursuit associated with the sciences of medicine, or with health problems.

To direct the work in an institution such as this College has come to be, and to fully develop its potentialities, there is needed a man conversant with academic traditions, trained in science, experienced as an executive, and capable of bridging the chasm which the years have worn and which now unhappily separates the medical investigators from the group of research workers dealing with the pharmaceutical and chemical aspects of medicinal products.

And Admiral William Clarence Braisted, President of the American Medical Association, who is pre-eminently qualified to render this exceptional service to the College and to pharmacy and medicine, has accepted the call of the presidency to carry to a splendid consummation the extensive educational program projected, and

the material development which it necessitates. His charming personality and his renown will be an inspiration. His past achievements guarantee success. Alumni, faculty and college officers stand ready to give him their enthusiastic support.

—The Site on the Parkway:—it will be secured. The New Buildings:—the plans are under way. The Money for this pretentious development in all its branches:—it will be forthcoming when needed. The Leader who can guide us to wider fields of service:—he has been found.

The vision of a greater Philadelphia College of Pharmacy and Science, a fitting memorial to the founders and to all who participated in the upbuilding of the College in the years past, will soon become an actuality.

J. W. S.

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#### EXAMINATION AS A MEASURE OF ABILITY.

No experienced teacher ever expects an examination or even a series of examinations, to yield mathematically accurate results in measuring the ability of a student. The values obtained are only relative and must be considered in connection with other factors in passing final judgment upon any applicant who is subjected to such a test.

An examination is sometimes a measure of capacity or of retentiveness or of concentration, if it follows close after the presentation of a subject, but it can never be considered as an infallible index of mental qualifications.

If this be true of specific examinations covering a single subject or a limited range, how much less value can be placed upon examinations which are known as "general information tests." And yet there is an element of value here which must not be overlooked.

Much comment has resulted the making public of a list of questions which it is said, has been used by Thomas A. Edison in passing upon applicants for positions in his employ. Many prominent educators and professional men have seen fit to criticize Mr. Edison and deride his plan as of no value for the purpose.

How do these individuals know Mr. Edison's purpose? He has not revealed it. His published comment which brought the storm about him was to effect that "college graduates are amazingly ignor-

ant." Perhaps this is so, and perhaps this fact is made plain by just such a test as Mr. Edison applied if rightly interpreted. The kind of questions used by Mr. Edison are apparently of the general information type. This type of questionnaire is found as one of the subdivisions of the Alpha Army Intelligence Test, to which a million or more American youths were subjected while in the training camps during the war.

Information for its own sake is of little value. It is ordinarily regarded as haphazard or casual as opposed to knowledge which is accurate and systematic. Learning is superior to information and is the result of study. Wisdom is said to be applied knowledge. Information therefore may be looked upon as an amorphous form of knowledge and as such is one of the fundamental factors of wisdom.

Exposure to sources of information does not always result in the infection of the individual, else proofreaders would be among the wisest in the land or the best informed, which they usually are not.

If one studies Mr. Edison's questionnaire, however, one is impressed by the fact that it can be resolved into a number of groups of allied or associated questions concerned with such subjects as physics, chemistry, geography, history and literature to mention the most outstanding.

Is it not possible, therefore, that Mr. Edison by picking out the answers to certain questions and groups of questions may be able to classify his applicants according to their predilections and hobbies? And is it not also possible that, when one finds a large number of applicants whose knowledge is so vague and incomplete that no single subject is even passably covered, a conclusion could be drawn similar to that expressed by Mr. Edison?

All of the critics of Mr. Edison's questionnaire have assumed that he was trying to find men who were capable of making a perfect mark. This is to be doubted. What he was probably trying to do was to find men who knew all about some one subject, and in addition had a fairly wide range of general information. A man who could answer all of the questions would probably be shunned by Mr. Edison himself.

Mr. Edison is too smart a man to waste time trying to find out unnecessary things. "Methinks there is a method in his madness."

CHARLES H. LAWALL.

## ORIGINAL PAPERS

## PELARGONIUM OIL.

PROFESSOR RICHARD KNUTH,

CHARLOTTENBURG, GERMANY.

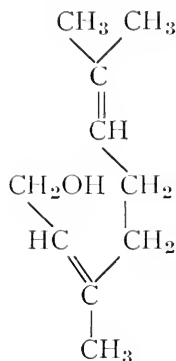
*(Continued From the May Number, Page 315.)*

## CHEMICAL CONSTITUTION OF THE PELARGONIUM OIL.

It is probable that the oil was produced first by Recluz, at Lyons, in 1819, by means of steam distillation (*Pharm. Jour.*, London, I, 11, 1852, p. 325). The knowledge of its constitution is, however, the result of the last thirty years. The reason for this is the complicated construction of most of its elements which, like many camphors, stand on the frontier between the acyclic and cyclic hydrocarburets. Up to now there are known to be contained in the pelargonium oil: the alcohols: geraniol, citronellol, linalol, isoamyl-alcohol; a paraffine; the terpenes phellandrene and pinene; a cyclic ketone; the menthone; the terpeneol; a blue-colored high-boiling potion, and different paraffine acids.

The geraniol,  $C_{10}H_{18}O$  represents the well-redolent part not only of the pelargonium oil, but also of the palmarosa-oil, the true rose-oil, and of many other etherial oils. Some of the secondary ingredients confer upon the oil the by-odor which distinguishes the pelargonium-oil from the true rose-oil. The geraniol itself was produced artificially for the first time by the firm Schimmel & Co., from the citronella oil. This method was protected by the German Imperial Patent No. 76,435. According to the accounts (Schimmel, Ber., 1894, I, p. 63; 1894, II, p. 77; 1895, I, p. 76), the pure geraniol is a colorless liquid of roseal odor, optically inactive, and with a specific gravity, varying from 0.882 to 0.885, at a temperature of 15° C. It boils at 230° C. In alcohol it is very easily soluble: in from 12 to 15 parts of a 50 vol.-per cent. alcohol. A disadvantage

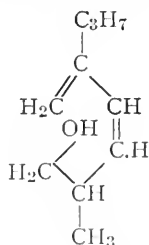
lies in its very easy oxydation, by which its specific qualities are partly changed.



GERANIOL ACCORDING TO TIEMANN AND SEMMLER.

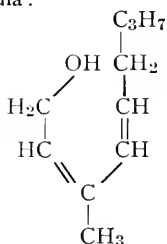
The history of geraniol is rather complicated. It was first pointed out by Jacobsen (Liebig's Ann. Chem., CLVII, 1871, p. 232), in connection with the oil of Andropogon. Later geraniol was found by Gintl (Jahresber. f. Chemie, 1879, p. 941) in the oil of pelargonium. Its constitution was explained by Semmler. Then the active element in the true pelargonium-oil was recognized by Monnet and Barbier (Comptes rendus, CXVII, 1893, pp. 1092-1094), as a specific alcohol of the formula  $\text{C}_{10}\text{H}_{18}\text{O}$  and which was identified with the rhodinol of the true rose-oil<sup>1</sup> (Conf. Germ. Imp. Pat. No. 80,007). From both oils they produced, by means of oxydation an aldehyde, the rhodinol  $\text{C}_{10}\text{H}_{16}\text{O}$ , a tetrasubbbromide  $\text{C}_{10}\text{H}_{18}\text{Br}_4\text{O}$  and a dichlorhydrate  $\text{C}_{10}\text{H}_{18}\text{Cl}_2$ . Markownikoff and

<sup>1</sup>The name is owing to Eckart (*Chemische Untersuchungen des deutschen und des türkischen Rosenöls*, Inaug. Diss., Breslau, 1891, p. 14). He accepted for his rhodinol the formula:



Reformatski <sup>2</sup> (Journ. prakt. Chem. Ser. 2, Vol. XXXXVIII, 1893, pp. 293-314) thought they had found in the true Bulgarian rose-oil an alcohol of the formula  $C_{10}H_{20}O$ , the roseol. This roseol of the rose as well as the rhodinol of the pelargonium should be different from the geraniol. For the rhodinol this difference was asserted for a long time by Barbier and Bouveault (Comptes rendus, CXVIII, 1894, pp. 1154-1157). They later gave more exact accounts concerning the constitution of the substance (Comptes rendus, CXIX, 1894, pp. 281-284 and 334-337; CXXII, 1896, pp. 529-531). Hesse (Journ. prakt. Chem., Ser. 2, Vol. L, 1894, pp. 472-479) believed to have found as the principal element of the Réunion oil and of the true German rose-oil, an alcohol, the réuniol, which should be, as well as the true geraniol, the true rhodinol of the French chemists. Erdmann and Huth (Journ. prakt. Chem., Ser. 2, LIII, 1896, pp. 42-46), and Erdmann (Journ. prakt. Chem., Ser. 2, LVI, 1887, pp. 1-47) denied the existence of the réuniol, which they identified with the rhodinol and also believed to be identical with the geraniol of Jacobsen. According to the researches of Bertram and Gildemeister it was finally found by Schimmel (Ber., 1895, I, pp. 37-39; 1896, I,

As Semmler accepted for his alcohol which he had found in the andropogon-oil the formula :



Poleck presumed (Verh. Ges. deutscher Naturforsch. u. Aerzte, LXIV, Vers. II, 1891, p. 77), just as Eckart (*Chem. Untersuchungen des deutschen und des türkischen Rosenöls*, in Ber. Deutsch. Chem. Ges., XXIV, 1891, pp. 4205-4210), that the rhodinol which Eckart had found in the true rose-oil and the geraniol were different. Compare also the previous remark of Poleck (in Ber. Deutsch. Chem. Ges., XXIII, 1890, pp. 3554-3555), in which he was inclined to identify the alcohol of the rose-oil and of the andropogon-oil (the geraniol of Semmler).

<sup>2</sup> Compare also the historical dates of the researches into the true rose-oil.



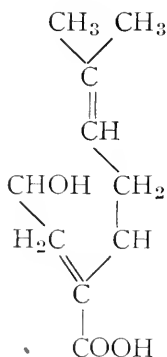
pp. 36-41), that rhodinol, roseol and réuniol had in common the possession of geraniol, to which was added a second alcohol, which later was determined by Wallach (Central Blatt, 1896, I, p. 809) as citronellol. As to the question whether the name of citronellol or rhodinol had the right of priority, there have been many disputes. The name of rhodinol had been claimed also for geraniol by Erdmann and Huth (see above); then by Poleck (Journ. prakt. Chem., Ser. II, LVI, 1897, pp. 515-519). The question had also been decided by Bertram and Gildemeister (Journ. prakt. Chem., Ser. II, LVI, 1897, pp. 506-514). The difficulties connected with the solution of this question may be seen from the following account of the two chemists cited. Rhodinol *Eckart* is a compound of from 20 to 25 per cent. of citronellol with from 75 to 80 per cent. of geraniol; rhodinol *Barbier and Bouveault* is identical with citronellol  $C_{10}H_{20}O$ ; rhodinol *Erdmann and Huth* is identical with geraniol  $C_{10}H_{18}O$ ; rhodinol *Tiemann and Schmidt* corresponds to 1-citronellol. Compare besides Bertram and Gildemeister (Journ. prakt. Chem., Ser. II, LIII, 1896, pp. 225-237), and Hesse (*ibid.*, pp. 238-241).

The geraniol was found up to now chiefly in the following oils: essence of acacia-blossoms (Schimmel, Ber., 1903, II, p. 15); essence of champaca-blossoms, prepared from *Michelia* species (Schimmel, Ber., 1907, II, p. 18); citronellol-oil, from *Andropogon nardus* L. (Schimmel, Ber., 1893, II, p. 12); citron-petitgrain-oil, from *Citrus limonum* Risso (Schimmel, Ber., 1905, I, p. 63); eucalyptus-oil, from *Eucalyptus macarthuri* H. D. et J. H. M. (Schimmel, Ber., 1907, II, p. 36), from *Eucalyptus maculata* Hook. (Schimmel, Ber., 1893, II, App. 18), from *Eucalyptus maculata* var. *citriodora* Hook. (Schimmel, Ber., 1890, p. 20, App. 18); geranium-oil (Gintl, Jahresber. Chem., 1879, p. 941); gingergrass-oil, from *Andropogon spec.* (Schimmel, Ber., 1904, I, p. 52); lavender-oil (Schimmel, Ber., 1904, I, p. 131); lemongrass-oil, from *Andropogon citratus* D. C. (Schimmel, Ber., 1894, II, p. 32); linaloa-oil, from *Bursera* and *Ocotea spec.* (Schimmel, Ber., 1904, I, p. 131); neroli-oil, from *Citrus bigaradia* Risso (Tiemann and Semmler, Ber. chem. Ges., XXVI, 1893, p. 271); orange-petitgrain-oil, from *Citrus aurantium* Risso (Roure-Bertrand Fils, Ber., 1904, II, p. 35); palmarosa-oil, from *Cymbogon Martini* Stapf (Jacobsen, Ann. d. Chem.,

CLVII, 1871, p. 232); rose-oil, from *Rosa damascena* Mill. (Bertram and Gildemeister, Journ. prakt. Chem., II, 1894, p. 184); ylang-ylang-oil, from *Anona odoratissima* (Reychler in Bull. Soc. chim., III, 1894, p. 1051); Yu-ju-oil, from a lauracea (Nagai in Monopoly Bureau, Government of Formosa 1914, Ref. in Schimmel's Ber., 1915, I, p. 43).

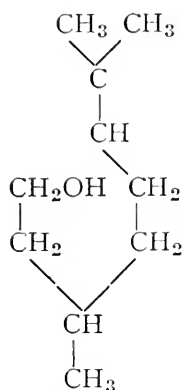
#### PHYSIOLOGICAL EFFECTS OF THE GERANIOL.

Hildebrandt (Arch. f. experim. Pharm. u. Pathol., XXXV, 1901, p. 121) injected geraniol into the blood of white mice and noticed already at an injection of 0.05 gr. signs of poisoning. As a product of transformation the same author found in conies a two-basic acid of the melting point of from 192° to 194° C., which may have the formula  $C_{10}H_{14}O_4$ , and which may be constructed in this way:



The isolation of L.-Citronellol,  $C_{10}H_{20}O$ , from the pelargonium-oil was accomplished by Tiemann and Schmidt (*Ueber die Verbindungen der Citronellol-reihe*, in Ber. Detsch. chem. Ges., XXIX, 1896, p. 921). It is the left form as also in the true rose-oil. In the true rose-oil its polarization amounted to 4° 20' in the 1 dm. reed., in the Spanish pelargonium-oil to 1° 12', in the African to 1° 20', in the Réunion-oil to 2° 15'.

Linalol,  $C_{10}H_{18}O$ , akin to the two preceding alcohols, was first identified by the chemists of the firm Schimmel & Co. (Schimmel's Ber., 1904, I, p. 51) in the Réunion-oil. Its boiling point under a pressure of 760 mm. is near 198° and 200° C. The proof of the existence of linalol in Réunion-oil was brought out by the same authors (Schimmel, Ber., 1910, II, p. 51).



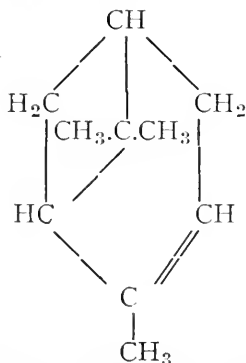
CITRONELLOL ACCORDING TO TIEMANN AND SCHMIDT.

Isoamylalcohol  $\text{C}_5\text{H}_{11}\text{OH}$ , with one of its isomerics was produced from the first runnings of the distillation of Réunion-oil (Schimmel, Ber., 1904, I, p. 51).

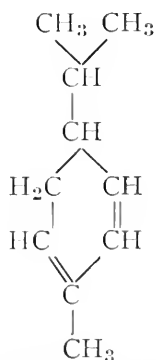
A paraffine was found by Barbier and Bouveault (Compt. Rend. CXIX 1894, p. 281). It was discovered in the remainders of the distillation in the vacuum. It is of crystalline quality and melts near  $63^\circ \text{C}$ . Its insolubility in 10 per cent. alcohol permits the conclusion that it is a paraffine.

Phellandrene  $\text{C}_{10}\text{H}_{16}$ , a monocyclic terpene. It was identified in the first runnings of Réunion-oil (Schimmel, Ber., 1904, I, p. 51).

Pinene  $\text{C}_{10}\text{H}_{16}$ , a bicyclic terpene. It was produced with the preceding from the first runnings of the Réunion-oil (Schimmel, Ber., 1904, I, p. 51).



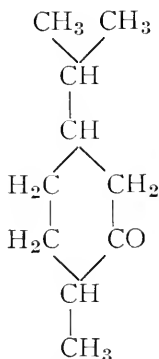
FORMULA OF PINENE ACCORDING  
TO WAGENER.



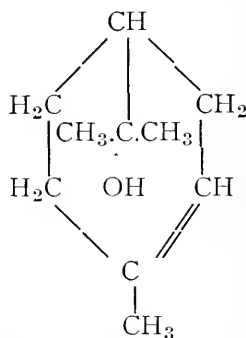
FORMULA OF PHELLANDRENE.

A terpineol  $C_{10}H_{18}O$ , a tertiary alcohol, was identified and isolated from the Réunion-oil by the chemists of the firm of Schimmel & Co. (Ber., 1910, II, p. 51; 1911, II, 46).

Menthone  $C_{10}H_{18}O$ , a cyclic ketone, was first found by Flatau and Labbé (Bull. Soc. chim., Paris, Ser. 3, XIX, 1898, pp. 788-790), then by the chemists of the firm Schimmel (Ber., 1904, I, p. 50), in the first runnings of the distillation, and in great quantity.



MENTHONE ACCORDING TO  
BECKMANN.



TERPINEOL.

A blue-colored high-boiling potion, as it exists in many etheric oils, is found also in the pelargonium-oil. Its composition is unknown. Probably it is the cause of the bluish-greenish color of the Réunion-oil. (Semmler, *Aetherische Oele*, III, 1906, p. 262.) Barbier and Bouveault were the first to call attention to it. They determined the boiling-point between  $165^\circ$  and  $170^\circ$  C., under a pressure of 10 mm.. In their opinion it is perhaps an ether of the formula  $(C_{10}H_{17})_2O$ .

Ester of geraniol and citronellol. The knowledge of this body is due to Barbier and Bouveault (Compt. Rend., CXIX, 1894, p. 281; cf. also the travels of the firm Schimmel & Co., Ber., 1894, I, p. 31). Both alcohols are partly bound to the following acids: a. Acetic acid,

$\text{CH}_3\text{COOH}$ . b. Isobutyric acid  $\left. \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right\} \text{CH} \cdot \text{COOH}$ . c. Isovaleric acid

$\left. \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right\} \text{CH} \cdot \text{CH}_2 \cdot \text{COOH}$ . d. Tiglinic acid  $\text{CH}_3 \cdot \text{CH} = \text{C} \cdot \text{COOH}$ . e. An

$$\begin{array}{c}
 | \\
 \text{CH}_3
 \end{array}$$

acid of the boiling-point at  $250^{\circ}$  C., which has probably the formula  $C_9H_{15}COOH$ .

In the Réunion-oil there are ester-contents of about 31 per cent.; in the Algerian oil, 29.1 per cent.; in the Spanish oil, 23.7 per cent.

The occurrence of pelargonium-acid in pelargonium-oil is very doubtful, though Pless (Semmler, *Aether. Ocle*, I, 1906, p. 766) believed to have found it there, and though it is also indicated by Gintl (Zeitschr. allgem. Oesterr. Apoth. Ver., XVII, 1879, p. 268). Charabot and Gatin (Journ. d'Alger. Imp., XVII, 1913, p. 290) also named citral  $C_{10}H_{16}O$ , an aldehyde, which is distinguished from geraniol by the possession of COH instead of  $CH_2OH$  in the final member. That substance had been isolated from the true rose-oil, but it is not known to me, whether it has been found in the pelargonium-oil.

DIFFERENCES IN THE COMPOSITION OF THE PELARGONIUM-OIL  
ACCORDING TO ITS ORIGIN.

According to Charabot (Bull. Soc. chim. sér. 3, XVII, 1897, pp. 489-492), the pelargonium-oil differs from the palmarosa-oil by the existence of active esters. He has shown that by addition of an alcoholic caustic lye polarization decreases in the pelargonium-oil, but not in the palmarosa-oil, which proves that the latter does not contain active esters. His experiments referring to the pelargonium-oil are found in the following table:

Origin of the oil.	Contents of geranyl-tiginate.	Alcohol $C_{10}H_{18}O$	Total alcohol.	Specific gravity at $15^{\circ}$ C.	Power of polarization 1-100 mm.	Power of polarization after saronification.	Decrease of the power of polarization.
Algeria, 1895,	25.31%	46.22%	62.74%	.896	$-9^{\circ} 50'$	$-5^{\circ} 46'$	$4^{\circ} 4'$
Algeria, 1895,	22.11	50.80	65.23	.899	$-9^{\circ} 20'$	$-4^{\circ} 24'$	$4^{\circ} 56'$
Algeria, 1896,	23.32	60.30	75.52	1.898	$-9^{\circ} 48'$	$-5^{\circ} 46'$	$4^{\circ} 2'$
Algeria, 1896,	25.66	41.80	58.55	.895	$-10^{\circ} 4'$	$-5^{\circ}$	$5^{\circ} 4'$
Algeria, 1896,	24.86	55.41	71.62	.894	$-9^{\circ} 10'$	$-5^{\circ} 8'$	$4^{\circ} 2'$
Réunion,	32.16	46.12	67.11	.8915	$-9^{\circ} 20'$	$-7^{\circ} 40'$	$1^{\circ} 40'$

According to these figures the Réunion-oil rather differs from the Algerian oil.

Tiemann and Semmler (Ber. deutsch. chem. Ges., XXIX, 1896, p. 924), indicate the following differences:

*Contents of Alcohol.*

Spain,	70 p. c.	65 p. c.	geraniol,	35 p. c.	cit.
Algeria,	75 "	80 "	"	20 "	"
Réunion,	80 "	50 "	"	50 "	"

Cf. also the account of the chemists of the firm Schimmel & Co., Ber., 1897, I, Anh., 23.

		<i>Power of polarization in 100 mm. conc.</i>	<i>Contents of esters calculated in geranyltiglinat.</i>
<i>Spec. gravity at 15° C.</i>			
Algeria,	0.892-0.9	6°30'-10° (1)	19-29 p. c.
France,	0.897-0.905	7°30'-9°30' (1)	25.28 "
Réunion,	0.889-0.893	8°-11° (1)	27-33 "

An analysis of Simmens (*Pharmac. Journ.*, XCI, 1913, p. 143) indicates the following values of geraniol and citronellol for the different oils:

	<i>Total-geraniol.</i>	<i>Citronellol</i>
Algeria,	69.3-79.5 p. c.	32-43 p. c.
Réunion,	69.7-73 "	44-51 "
Corsica,	69.8 "	30.3 "

Another account (*Perfum. Record*, IV, 1913, p. 328, says that by the methods of acetic acid and formic acid the following values had been found in six different geranium-oils, of which, however, the two last must be referred to cymbogon species.

	<i>Total-geraniol.</i>	<i>Citronellol.</i>
France,	72.7 p. c.	39.8 p. c.
Algeria,	74.1 "	32.9 "
Réunion,	73 "	44.3 "
Corsica,	73.3 "	45.9 "
Asia,	72.1 "	51 "
Asia,	69.1 "	62.3 "

The analysis of the pelargonium-oil which has been produced in Sicily gave, according to Umney and Bennet (*Pharm. Journal*, LXXV, 1905, p. 860; *Chemist and Druggist*, LXVII, 1905, p. 970), the following results: Geranyltiglinat 35.6 per cent., total-geraniol 71.9 per cent. The contents of esters were greater than in French and Algerian oils and almost equaled those which had been observed in Réunion-oil.

ALTERATIONS OF THE CHEMICAL COMPOSITION OF THE OIL THROUGH  
CHANGE OF WEATHER.

Charabot (Bull. Soc. chim., sér. 3, XXIII, 1900, pp. 922-928) examined two oils, which had been produced on July 18th and August 21st. The examination showed that specific gravity, polarization and contents of esters showed an increase, the contents of free acids and free alcohols, however, a decrease. The total contents of alcoholic components, however, was greater in the latter case. The quantity of citronellol seemed, according to Charabot, to be greater in proportion to geraniol. According to Jeancard and Satie (Bull. Soc. chim., sér. 3, XXXI, 1904, pp. 43-49), cold nights reduce the contents of alcohol. This decrease is, however, not the result of an intensive production of esters, but only to a decrease of oil. The contents of geraniol becomes smaller, that of citronellol increases in proportion to geraniol. While in many other oils, such as the neroli- and the petitgrain-oil the decrease of free alcohols is compensated by a greater production of esters, here the loss touches only the geraniol, whereas the citronellol increases slightly.

FALSIFICATION OF PELARGONIUM-OIL BY MODERATE CHEMICAL DRUGS.

In most cases they can be recognized by the odor; but often they imitate well the weight of the oil. In literature there are found accounts of falsification by means of the following substances:

Dimethylsulphide (Schimmel, Ber., 1909, I, p. 50); Aethyloxalate (*Perfum. Record*, 1911, II, p. 83); diphenylmethane (Charabot and Gatin, Journ. d'Agric. trop. XIII, 1913, p. 294); ester of benzoic-acid (Schimmel, Ber., 1905, II, p. 33); Aethylphthalate up to 20 per cent. (Schimmel, Ber., 1913, I, pp. 59-60); gurjunbalsam-oil, the oil of an East-Indian Dipterocarpus, up to 30 per cent. (Schimmel, Ber., 1908, I, p. 53; 1911, II, p. 47); derivatives of the lemon-oil (Charabot and Gatin, l. c., p. 294).

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## COMPARATIVE RESEARCHES ON THE METHODS PROPOSED FOR THE ESTIMATION OF GLYCYRRHIZIN IN LICORICE ROOT AND IN LICORICE EXTRACT.

By ARMIN LINZ.

(*Prize Research of the Hagen-Bucholz Foundation; 1913-1914.*)  
(*Archiv der Pharmazie*, 1916, Vol. 254, 65-134, and 204-224.)

TRANSLATED BY DR. PERCY A. HOUSEMAN. APRIL, 1921.

For a long time past, workers have concerned themselves with a large number of researches and publications on the constituents of licorice root and extract. As early as about 1800, Pfaff, Hermbstädt and Schwartze published statements on the composition of licorice root and extract, and also made known the characteristic precipitates which various reagents produced with an infusion. In the succeeding decades, the literature on this subject attained a considerable volume. All of these researches, however, up to about 1880, propose only the isolation of the characteristic ingredient of the root and extract, without placing any emphasis on a quantitative determination of it. Although for this reason, the above-mentioned researches have no direct connection with the methods used for the determination of glycyrrhizin, still I deem it necessary to give a survey of them. In the first place, there is naturally a certain dependency between the first experiments for the isolation of a substance and its quantitative determination; further, such a summary, taking into consideration all the papers which have appeared, has not hitherto been attempted.<sup>1</sup> The short summaries which precede the researches of Tschirch, Rasenak, Cederberg and Gauchmann, are incomplete, and are also partly erroneous.

In Appendix A is given a list of all the researches which are concerned with the ingredients of licorice root and extract, their chemistry and their quantitative examination. The claim may be made for this collection that it takes account of all the more im-

<sup>1</sup> The contents of these publications are given in the original dissertation in adequate fashion. At this time, however, it will suffice to communicate the author's results concerning the quantitative examination of licorice extract and root, and for the rest, to refer to the bibliography in Appendix A.—The EDITOR.

portant work published on this subject. Such a list has not been given before. The reviews in the older works such as Flückiger's "Pharmakognosie," Husemann's "Pflanzenstoffe," Tschirch's "Handbuch der Pharmakognosie," Dragendorff's "Die Heilpflanze," and Wehmer's "Pflanzenstoffe," are far from complete. Further, since the "Jahresbericht der Pharmazie" has not noted all of the articles, it was only possible to make such a list after examining all of the journals concerned.

Through the kind offices of several gentlemen, it was possible for me to examine nearly all of the articles in the original. I was also able to work on nearly all of the original articles in foreign journals, thanks to the use of the journal catalog of the "Auskunftsstelle deutscher Bibliotheken" now in the press, as well as the use of the library of the "Deutschen Apotheker-Vereins," and of the "Reichsgesundheitsamtes." In the case of those publications which I could not see in the original, I have used those abstracts which were available to me.

#### THE QUANTITATIVE DETERMINATION OF GLYCYRRHIZIN IN LICORICE.

The idea of determining the glycyrrhizin content, and of using it for the evaluation of licorice, belongs to Rump. As I have already indicated, he made the following statement in 1855: "The value of licorice is best determined from its content of glycyrrhizin, as is that of opium from its content of morphine." This statement did not remain uncontradicted. Shortly afterwards, Hager claimed the contrary. In spite of that, however, he stated there should be at least 10 per cent. glycyrrhizin in licorice extract. The next decades brought forth a large number of proposals for the quantitative determination of glycyrrhizin, from which it must be deduced that this determination was of value for determining the quality of any variety of licorice. In later years, however, more attention has been given to the sugar determination. This is justified. Outside of the obvious estimations of the soluble and insoluble portions, and of the ash, the determinations of glycyrrhizic acid and sugars are indispensable for a correct valuation. For example, by determining the glycyrrhizin alone, one could not detect the frequently-occurring adulteration with sugar, of an extract containing much glycyrrhizin. For this reason many of the later workers on this subject have taken up determination of sugars. I would only name here Houseman, Telle, Parry, Tschirch, etc.

A chronological list of the methods of glycyrrhizin determination published to date is collected at the close of this article under Appendix B.

A number of proposed methods, particularly those given in general works, are taken in part from other sources and appear, sometimes under other names, as original determinations. I found, for example, the method proposed by Diehl, under the name of Prolius in Hager-Fischer-Hartwich's "*Handbuch der Pharmazeutischen Praxis*," 1896. Hager's *Handbuch* has the method of Haffner in the supplementary volume. König's "*Nahrungs und Genussmittel*," 1, p. 1065, has reproduced the method of Kremel.

In the list in Appendix B I have only included original methods.

One can see how the glycyrrhizin content of licorice varies with the large number of quantitative methods employed. Glücksmann found in one kind of licorice, no glycyrrhizic acid at all, and others claimed to have found amounts up to nearly 30 per cent. Not only in different kinds, but also in the same kind at different times, have large variations in the glycyrrhizin content been found, a fact which finds its explanation in the very primitive methods of manufacture which are even yet partly used. The desire, which has often been expressed, to establish in the Pharmacopœia a lower limit for the glycyrrhizin content, or to describe the preparation in the Pharmacopœia regulations, is justified on these grounds.

From the very few comparisons of different methods hitherto available, it is to be seen that, by the many methods proposed, results differing largely from each other are obtained. I would here quote Erikson, who obtained 16.5 per cent. and Cederberg, 14.3 per cent. glycyrrhizin, even from the same extract. Glücksmann obtained 8 per cent. ammonium-glycyrrhizinate from an ammoniacal extract, and only 2 per cent. from an aqueous extract. Haffner, using Helfenberg's method, obtained 4.3 per cent., Kremel's method 3.1 per cent., and Diehl's method 6.4 per cent., using the same licorice extract for all. Haffner has compiled interesting tables in which he believes he demonstrates a connection between the extraction liquid, the method of purification, and the degree of purity of the glycyrrhizic acid obtained and weighed.

These results, which are so poorly comparable, justify the conclusions that the question of the method of glycyrrhizin determination is not yet cleared up. This fact, combined with the necessity of

such a determination, gives to the Foundation Research of this year great practical value.

Various workers in this province have designated as "thankless," their activities with glycyrrhizin, not only in the matter of ultimate analysis, but also from a quantitative-analytical point of view. This is easily understood, particularly in the latter respect. A pure glycyrrhizin, or an equivalent compound, can, in my opinion, not yet be obtained quantitatively. One only obtains a more or less impure acid or derivative, with varying losses.

#### INTRODUCTION TO QUANTITATIVE DETERMINATIONS.

Before I enter into control experiments of the individual methods proposed, and the results obtained, I should like to discuss here some fundamental questions which are of common importance to all or many of the methods proposed. I think I can, by this means, avoid unnecessary repetition.

In the first place may be mentioned the influence of the liquid which is used as a solvent for the licorice extract. Further, account should be taken of the acid used for precipitation. Then, the solubility of the glycyrrhizic acid in the precipitant, and in water, and the resultant losses must be investigated. And, finally, account must be taken of the degree of purity of the substance weighed. As regards the many questions which apply only to individual determinations, I shall consider these under the respective methods.

1. *The Liquid Used to Dissolve the Licorice Extract.*—The first proposals are, naturally, to dissolve the licorice in water, but it was found that this solution is extremely difficult to filter. In order to avoid this trouble, Diehl proposed, in 1883, to add an equal volume of alcohol after dissolving in water, and then to filter after settling. It is interesting that Diehl emphasized this proposal, on the ground of the easier filtration achieved. However, he not only achieved this practical object, but also obtained a greater purity in the acid which is separated later. By the addition of alcohol, the gummy and mucilaginous substances, which are present in considerable quantity, and which would otherwise pass into the filtrate, are precipitated. In the subsequent precipitation, one also naturally obtains a purer glycyrrhizic acid. In any case, the addition of alcohol to the aqueous extract must be regarded as an improvement, especially since no loss

of glycyrrhizin can, in general, occur. Under these circumstances, it is remarkable that since Diehl, and also quite recently, methods have been published which use no alcohol. The latter are, without doubt, inferior to those using alcohol.

Rump in 1855 appears to have been the first to propose an ammoniacal solvent for licorice extract. As I already mentioned in the introduction, he deduced, from the fact that the matters insoluble in cold water yielded a certain amount to ammonia, that there was present a glycyrrhizin soluble in water, and one soluble only in ammonia. Schroeder also, in 1883, emphasizes the difference between soluble and insoluble glycyrrhizin. I consider this ammoniacal extraction not the correct method.

In the introduction, I have mentioned that Tschirch considers the "glycyrrhizin" of the root present as a potassium and calcium salt of glycyrrhizic acid. He arrived at this view on the basis of the following experiment: A saturated aqueous infusion of the root was treated with an equal volume of alcohol, filtered, and to the filtrate three times the volume of absolute alcohol added. The glycyrrhizin compounds were thus precipitated. The precipitate was filtered off, dissolved in glacial acetic acid, and purified by crystallization. Tschirch obtained two kinds of crystals, which showed by qualitative analysis, the presence of potassium and calcium.

The statement of Flückiger in 1867, that "glycyrrhizin" is the ammonium salt of the acid, has been doubted by many, among them Sestini. Tschirch considered that he has definitely disproved this view, since in the precipitate mentioned above, he found no ammonium compound. The opinion which has been published in one paper, that the magnesium salt of the acid is concerned, is in itself not improbable. It has, up to the present, not been contradicted. In addition to the combined acid, the root is said to contain, according to statements in the literature which agree on this point, also small quantities of free glycyrrhizic acid.

In the preparation of licorice extract, which is, in part, still very primitive (see Tschirch's "Handbook" and Anselmino-Gilg "Commentary"), the root is boiled with water. The small quantities of the free acid are certainly neutralized by the constituents of the well-water, or by salts of the root, so that it may be taken as established, that glycyrrhizic acid occurs in licorice extract only in combined form. Without wishing to decide the question of what compounds

are present in the extract, I will here only consider the possibility that it can be a question of a potassium, calcium, magnesium, and ammonium salt. The potassium and ammonium compounds are very easily soluble in water. The literature says nothing about the magnesium compound, which does not appear to have been prepared yet. It may, however, be assumed from the nature of magnesium salts, that the glycyrrhizinate is easily soluble. As regards the calcium salt, Sestini reports that it is difficultly soluble in water. When one remembers, however, that by the various methods, only very trifling quantities of calcium salt are present to be dissolved, one may assume that the calcium glycyrrhizinate will be dissolved in the amount of water used in the determinations.

All possible compounds present in licorice extract as "glycyrrhizin" are therefore water-soluble for the purposes of our practical testing comparisons. A free acid which must be made soluble by alkali, is not present. It is therefore superfluous to add ammonia to the solvent. Such an addition is not only unnecessary, but even undesirable, for Haffner has proved that calcium glycyrrhizinate is extremely difficultly soluble in ammonia. There is another important fact which argues against such an extraction. It is proved that ammonia dissolves a considerable quantity from the residue insoluble in water. If it be possible to dissolve out with water the total glycyrrhizic acid compounds (and I am of the opinion that this can be done, provided, of course, that not too small quantities of water are used), then it is incorrect to use ammonia, and thus extract still more from the otherwise insoluble matter, which does not contain glycyrrhizin compounds. The more "non-glycyrrhizin" the filtered extract contains, the more impure must the precipitated glycyrrhizic acid be. Or, positively stated: The precipitated glycyrrhizic acid is the purer, the greater the insoluble residue, presuming, of course, that the total glycyrrhizin compounds have been extracted from it. I will merely mention that an ammoniacal licorice extract is appreciably more difficult to filter than an aqueous extract. The above remarks explain why I obtain higher values in using ammoniacal extracts, than in using pure water in the control experiments to be discussed later. This excess is, however, only obtained at the cost of the purity of the weighed product. For all of these reasons I hold an ammoniacal treatment of the original licorice extract to be incorrect.

As a third extraction-liquid, Haffner proposes a mixture of sulphuric acid and alcohol. Alcohol alone dissolves practically nothing from licorice extract, since all of the glycyrrhizin compounds are very difficultly soluble or almost insoluble in alcohol. By the addition of sulphuric acid, the glycyrrhizin compound is decomposed, and the free glycyrrhizic acid is formed, which is easily soluble in the mixture of alcohol and sulphuric acid. Haffner, therefore, avoids the question of the solubility of the various compounds, by setting free the glycyrrhizic acid. The question as to whether this treatment dissolves out all of the glycyrrhizin, I can answer unconditionally in the affirmative. It can hardly be doubted that the total glycyrrhizin salts of licorice are decomposed by sulphuric acid or that the free glycyrrhizic acid so liberated is soluble in the sulphuric acid-alcohol mixture. There is therefore no objection to Haffner's proposal from a quantitative point of view.

In order to determine whether there is anything soluble in ammonia in the dry residue from Haffner's method, I extracted exactly 5 grams of the insoluble matter with ammoniacal water. Even after the third extract, the decanted liquid was quite black. From the united evaporated extracts, I was able to obtain 0.189 grams ammonium glycyrrhizinate in the usual analytical way. Since this 5 grams residue corresponds to about 10 grams of original licorice extract, there is found by this method, in the residue from Haffner's method, nearly 2 per cent. of "ammoniated glycyrrhizin" which contains no glycyrrhizic acid, but which, by an ammoniacal extract of licorice would probably be obtained as an impurity in the acid, and would be weighed as glycyrrhizic acid.

I would, therefore, state my opinion on the various proposed extraction-liquids as follows: Both the aqueous extract followed by alcohol, and also the alcohol-sulphuric acid extract, give good results; but, on the contrary, the ammoniacal extract is inferior to both, because it gives values which are higher than the correct figure.

2. *The Solubility of Glycyrrhizic Acid.*—As far as I could determine, Haffner, in 1899, was the first to make experiments on the solubility of glycyrrhizic acid. Maisch, in 1884, in commenting on the method proposed by Schroeder, showed, that such a solubility determination is very desirable. Haffner shook up glycyrrhizic acid with excess of water, and determined the solubility by evaporation. He found the proportion 1:60, which corresponds to 1.67 per cent.



He emphasizes particularly, that he did not make this experiment with pure acid, for the reason that such a substance is not obtained in the quantitative determination. Capin in his dissertation, made detailed researches on the solubility determination, but the conclusions which he drew are partly incorrect. I will here only consider his solubility determinations. I will speak of their application to his proposed method of determining glycyrrhizic acid when I discuss that subject.

When one adds sulphuric acid to precipitate an extract of licorice or a glycyrrhizin solution, the supernatant liquid remains colored. From this Capin concludes: "If now the total glycyrrhizic acid had been precipitated by the addition of sulphuric acid, it is evident that the liquid, after filtration, would not show the least color." This conclusion is incomprehensible. It would be true, and only then conditionally, if pure glycyrrhizic acid were colored, or better, black. But Capin has written the above statement in spite of having read the researches of Tschirch! In order to determine its solubility, Capin shakes up 25 grams glycyrrhizic acid (impure, washed with water, alcohol and ether) with 200 cc. water, and allows the liquid to stand for 24 hours. He then filters, and cools the clear solution to  $0^{\circ}$  in a mixture of ice and salt. A further precipitate is formed, which is filtered off through a funnel kept at  $0^{\circ}$ . He then dries 20 cc. of this filtrate to constant weight, and obtains 0.110 grams of residue which corresponds to a content of 0.55 per cent. (not 0.575 per cent., as is stated in Capin's dissertation in consequence of a misprint). Under the same experimental conditions, he then determines that the solubility factor at  $15^{\circ}$  amounts to 0.575 per cent. These two numbers, as shown above, have become mixed, and the error has been carried into the French journals in part, for example, in the *Repertoire de Pharmacie*, III, 24, p. 14. In consequence of this error, Anquet has called the attention of the author to the unusual procedure in prescribing a temperature of  $0^{\circ}$  although the solubility according to his results, is higher at  $0^{\circ}$  than at  $15^{\circ}$ . A comparison of the dissertation with the Bulletin des Travaux de la Société pharmaceutique de Bordeaux shows at once that it is only a question of an oversight or a printer's error. The conclusions of Anquet are therefore not justified.

The observation of Capin, that a clear solution, from which the glycyrrhizin has been precipitated, separates a further quantity of the

acid by cooling to  $0^{\circ}$ , is confirmed by myself. I noticed it particularly in the method of Evans' Sons, which will be treated later. It may, therefore, be taken as proved by this simple experiment, that glycyrrhizic acid is less soluble in water at  $0^{\circ}$  than at  $15^{\circ}$ , from which one deduces the obvious application to the analytical method. A similar method for determining the losses in the glycyrrhizin determination, due to the solubility of the acid in water, is described by Durier.

He dissolves the glycyrrhizic acid, which he had precipitated in previous experiments, in 25 cc. water, and precipitates with hydrochloric acid. He filters and weighs the residue. The difference between glycyrrhizic acid used, and that finally weighed is considered by him as the solubility number in 25 cc. of water. Here also an error is involved. Durier does not determine the solubility in water, but in acidified water. These two solubility numbers are entirely different! In discussing Durier's work I shall go into this in detail.

We see that Haffner, Durier and Capin have concerned themselves with the solubility of glycyrrhizic acid, and that all three, under different experimental conditions, arrived at quite different results. Under these circumstances the question presents itself: Have these experiments any object? Theoretically it must be obviously answered in the affirmative, but it is otherwise with the practical side of this question as regards the application for the present work. First of all the question must be answered: Shall the solubility of the chemically pure or of the impure acid be investigated? Haffner voices his views as follows: "Chemically pure acid does not enter into the practical question, therefore for the solubility determination I use the impure acid." I am of the same opinion. Nobody has yet succeeded, and in my opinion never will succeed, in weighing approximately pure glycyrrhizic acid quantitatively. I therefore consider it of no practical value to determine how much of the pure acid dissolves in water, since one always works with impure acid. One always weighs "glycyrrhizin plus impurity." Of this mixture the pure acid, or the impurity, or a portion of both may dissolve in water. Since one weighs the impure acid it would be inaccurate to take into account only the solubility of one constituent of the mixture of glycyrrhizic acid plus impurity, and to neglect that of the other. Judging from this line of thought, one should determine the solubil-

ity of the impure acid. But here one encounters manifold difficulties in its accomplishment.

Haffner, Capin and Durier were each working with different materials. It is therefore necessary to take into account the degree of purity or impurity. It would not be fair to judge the results of an experiment on one acid from the results on other acids. If one wishes to obtain exact results and to add the percentage solubility to the value found in a glycyrrhizin determination, one would have to do a solubility determination for every kind of glycyrrhizin determination. In that case it would be necessary to dry the glycyrrhizin at a 100° to constancy, which treatment would undoubtedly change its physical properties. I would only quote one example—the change in its solubility in alcohol, if one dries glycyrrhizic acid at room temperature. It would be unreasonable to assume that the washing of the precipitated wet acid entails the same losses as result from the use of the completely dried acid. In spite of this, it has been proposed to compare these results!

The attempt which Capin and Durier have made, to correct for the losses due to washing in the respective analytical procedures, by the addition of a number to the glycyrrhizin value obtained, which shall be valid for all kinds of licorice is, in both cases, not only inapplicable on account of inaccurate experimental conditions which result from the solubility determination, but is also open to fundamental objections. The values which both have found, refer, naturally, only to saturated solutions, which, however never come into question, in a glycyrrhizin determination. In the latter case, it is a question only of washing the precipitated acid with water, and of the solubility of the same in the acidified liquid in contact with it. It is, therefore, quite clear that totally different conditions exist, and that they cannot be compared with one another. The experiment of Capin and Durier will therefore never be suitable for quantitative work. A different method which I will mention below might be more applicable.

Summarizing, I would therefore state:

1. It is of no value for the practical glycyrrhizin determination to determine the solubility of the pure acid.
2. A determination of the solubility of the impure glycyrrhizic acid cannot be carried out under conditions which are equivalent or similar to those of a glycyrrhizin determination.

If then the quantitative solubility values seem to have no value, it becomes all the more important to establish the following facts:

Glycyrrhizic acid is only very slightly soluble in water, and less so in water of 0° than at 15°.

Glycyrrhizic acid is also somewhat soluble in acidified water, but noticeably less so than in pure water.

3. *Experiments to Establish Quantitatively the Losses Caused by the Solubility of Glycyrrhizic Acid.*—The only procedure which has up to now attempted to establish in a glycyrrhizin determination, the losses due to solubility, and to give a figure for them is that of Cornimboeuf. I will discuss it at this place since Cornimboeuf only treats of the estimation of glycyrrhizic acid in ammoniated glycyrrhizin, which is not the purpose of this work. Cornimboeuf filters the glycyrrhizin which has been precipitated with sulphuric acid, and dissolves it in ammonia. He evaporates the supernatant liquid, together with the wash waters almost to dryness, kneads the tough black residue successively with 10, 10, and 5 cc. of water, filters the wash water, dissolves the remaining second portion of glycyrrhizic acid in ammonia, unites the two ammoniacal glycyrrhizic solutions and dries them to constant weight. I do not consider this procedure free from objection.

Independently of Cornimboeuf, but in a similar way, I have often attempted to determine at least approximately, the quantitative losses of glycyrrhizin, but I always made the same observation. As the evaporation of the mother liquid and the wash waters progressed, the glycyrrhizic acid separated out at first in brown flakes, which in the course of further evaporation became deep black. They proved to be very difficultly soluble, and partly quite insoluble in ammonia. When one remembers that during evaporation, the water is volatilized, but not the sulphuric acid used for precipitation, and that at the end the glycyrrhizin in the mixture is in solution in a very strong sulphuric acid, one has a sufficient explanation for this condition. Under the influence of the strong acid, decomposition has taken place, and partial carbonization will occur, especially when the evaporation is carried almost to dryness according to Cornimboeuf's method.

Naturally the kneading of the sticky acid with 25 cc. water also causes losses, but unfortunately such losses cannot be avoided in the glycyrrhizin determination.

I have found a different way, which in my opinion is suitable to determine, fairly accurately, the losses in glycyrrhizic acid.

I evaporate the mother liquor and wash waters to a syrup after saturating the free acid with ammonia. I transfer this saturated solution of ammonium glycyrrhizinate, and ammonium sulphate or chloride, to a narrow glass cylinder graduated in  $\frac{1}{2}$  ccs. The solution is then brought to such a volume, that for every gram of licorice extract taken, four grams of solution result. I then precipitate the glycyrrhizic acid with sulphuric acid, of which for every gram of acid I used ten drops. After standing twelve hours, the liquor was filtered through a fluted filter, 5 cm. diameter, the acid was collected on the filter paper and washed with 2 per cent. sulphuric acid at 2° C. For this purpose I used 5 to 10 cc., according to the quantity of the precipitate, which is then washed with 5 to 10 cc. of water saturated with ether at 2° C., and the residue is dried over sulphuric acid in a vacuum desiccator. The filter is then extracted with hot 95 per cent. alcohol, the alcoholic solution is evaporated, and the residue weighed as glycyrrhizic acid. By my process I have excluded the possibility of decomposition. Ammonium glycyrrhizinate is so stable that it stands evaporation even to dryness. It is unfortunately not possible to avoid losses, through solubility in the supernatant liquid from the precipitation, but they are quite small. The washing of the glycyrrhizic acid also causes losses, but these are likewise quite small. By following the above experimental procedure I believe that I have obtained practical quantitative results which are interesting in showing the losses sustained by the individual methods.

4. *The Acid Used for Precipitation.*—Glycyrrhizic acid is a weak acid, which is precipitated by most other acids. For the quantitative determination of glycyrrhizin, it is naturally of value to know which acid is the most suitable for precipitation. The precipitants used in the methods to be investigated are sulphuric acid, hydrochloric, and absolute alcohol. I made comparative investigations with sulphuric, hydrochloric, boric, oxalic, tartaric, phosphoric and formic acids. I made such a solution of licorice that after filtering, the soluble portion of the licorice was present in the proportion 1:9. Of this solution 10-gram portions were treated, in wide test tubes, with 2.0 cc. dilute sulphuric acid, 3.0 dilute hydrochloric acid, 5.0 phosphoric, 15.0 hot saturated boric, 15.0 tartaric (5 per cent.), 3.0 nitric, 10.0 formic. The contents of each tube was made up to 25.0 cc. By

a control experiment beforehand, I had convinced myself that the quantities used for precipitation were sufficient. After standing 24 hours, and filtering, these control experiments gave no further precipitate when more of the same precipitant was added. The liquids were filtered after standing 24 hours. The tartaric acid had gelatinized the contents of the tube, so that one could turn it upside down without anything running out. Therefore, it cannot be used for precipitating any better than acetic acid, in which glycyrrhizic acid is easily soluble. The colors of the filtrates, and also that of the precipitated acid, show great variability. The filtrates from boric and phosphoric acid precipitations were light brown; those from sulphuric, hydrochloric and nitric acid, more or less dark brown to black. The precipitated acid was black and uninviting, except with oxalic acid, in which case it had a light grey color, which may be ascribed, probably, to the precipitated calcium salt. To each of the clear filtrates, I then added 2 cc. dilute sulphuric acid. After standing for 10 hours, it was found that all of the solutions, with the exception of the sulphuric and hydrochloric, had precipitated some more glycyrrhizin. The amount of additional precipitate was only slight in the case of phosphoric acid, nitric acid, and oxalic acid, but was considerable in the case of boric and formic acids. Reaction between the first precipitant and the small quantity of dilute sulphuric acid need not be feared, and is not concerned in the precipitation. I arrived at the same conclusions through a second experiment. I prepared a purified glycyrrhizic acid from an alcoholic extraction of the dried acid, and shook up with water, a larger quantity than could be dissolved. To 20 cc. portions of the clear filtrate in large test tubes I added 2 cc. of various acids. Sulphuric, hydrochloric and phosphoric acids gave a turbidity immediately, oxalic and nitric acids only after some time and finally formic acid also gave a trifling turbidity. The liquid was filtered after 24 hours, and on adding 2 cc. sulphuric acid to the still more dilute glycyrrhizin filtrate, after standing 10 hours a flocculent precipitate was formed in all of the solutions, with the exception of those containing hydrochloric and sulphuric acids. From these two simple experiments only one conclusion is possible: Sulphuric and hydrochloric acids react more sharply than other precipitants. In order to decide which of these two acids works the more strongly I proceeded as follows:

A saturated solution of glycyrrhizic acid was diluted, in one case,

with twice, and in another case, with three times the volume of water, and to 10 cc. portions of these solutions were added 1 cc. dilute sulphuric, and 1 cc. dilute hydrochloric acid. After several hours, all four test tubes showed light flocculent, gelatinous precipitates. From another saturated solution, in order to avoid possible decomposition, I made a dilution in the proportion of 1:2½, and added to each 10 cc., 1 cc. of the acids. This time, the hydrochloric acid solution remained quite clear, even after 24 hours, while the sulphuric acid solution gave a very light, but positive turbidity. This proves that sulphuric acid unquestionably precipitates glycyrrhizic acid quantitatively, better than hydrochloric, and that the glycyrrhizin is more difficultly soluble in the former than in the latter. Sulphuric acid is therefore certainly the most suitable acid for precipitation. In these experiments, I have intentionally avoided any quantitative determination, since it is here a question of only very small quantities of a material which is not uniform. Under these circumstances, differences in the third decimal place can hardly have any significance. I believe, however, that for practical purposes of a glycyrrhizin determination my two experiments are sufficiently convincing. From them may be stated that only sulphuric and hydrochloric acids may be considered as precipitants, and that the first acid works more exactly and sharply. All other acids cannot be used.

5. *Experiments to Establish the Purity of the Acid Weighed.*—

Since, by the various determinations, acids or salts of various degrees of purity are weighed, it is not sufficient, in criticising glycyrrhizin determinations, to compare the quantities obtained and weighed. Account must also be taken of the purity of the same. The only attempt to do this has been made by Haffner. He prepares the barium salt, and determines the barium by evaporation with sulphuric acid, weighing the barium sulphate, and has in this manner a method for determining the purity of the glycyrrhizic acid. If I would now attempt, in the present work, to determine the degree of purity of the acid, I could not, of course, at once accept Haffner's methods. Haffner's acetone extracts have for their object a purification of the acid which is quite foreign to my intention, and in this case would be quite inaccurate. I tried all kinds of variations of Haffner's procedure without attaining my object. I should like, first of all, to mention a few facts established in this connection. A filtered solu-

tion of ammonium glycyrrhizinate leaves an insoluble residue, after it has been evaporated, dried at a  $100^{\circ}$ , and taken up in water again. Ammonium glycyrrhizinate which had been dried at  $100^{\circ}$  (as it is weighed), cannot, without purification, be converted to the barium salt. Glycyrrhizic acid dried at  $100^{\circ}$  cannot be redissolved in 95 per cent. alcohol without leaving a residue. Glycyrrhizic acid itself cannot be converted to the barium salt without purification. In the barium salt obtained, the barium could be determined, and from that, an indication of the purity of the salt could be obtained. But this does not result in even an approximate estimate of the purity or impurity of the acid or ammonium salt weighed. To all these facts and thoughts can be added the same objections made against the purity test of Haffner's.

I therefore come to the conclusion that it is not possible, according to Haffner's proposal, or any other methods, to determine the degree of purity of the acid, even approximately. I cannot accept the degrees of purity set up by Haffner for the various acids. According to his own results, he can hardly accept them—and if he does, they do not give a true picture—and he offers no other method. Although such an exact determination of the degree of purity is very desirable and indispensable for a conclusive estimate of the individual methods proposed, one is left to rely only on the taste and appearance as a measure of control. It is shown that the ammoniacal extract undoubtedly gives a less pure acid than an aqueous extract, and for the same reason the use of alcohol is to be preferred to a purely aqueous solution. From the appearance of the acid weighed, it is to be seen that a purification with alcohol according to Diehl is important. The ammonium glycyrrhizinate obtained by Diehl's procedure is of a light brown color, while that from the other methods is colored dark brown.

#### QUANTITATIVE CONTROL OF THE PUBLISHED DETERMINATIONS OF GLYCYRRHIZIC ACID.

##### *The Licorice Used for Control Experiments.*

In order to carry through a critical work such as the present, it was necessary to investigate only one kind of licorice extract, so that the results obtained could be compared with one another: Although it might appear desirable to investigate the action and accuracy of the individual methods proposed, on different kinds of



licorice, say a very good one, a medium quality, and a very bad one, the work necessary to carry through this idea would spread beyond the limits of this task. Above all, time would not permit of exact and exhaustive treatment. With this thought in mind, after trying various kinds, I decided to use the Baracco brand for my control experiments. I obtained this from the firm of Caesar & Loretz. The method of our Pharmacopœia gave the following results:

Residue insoluble in water was 31 per cent.

11.4356 g. of licorice lost 1.8777 g. when dried at a 100° to constant weight, equivalent to 16.42 per cent. moisture.

The ash was 9.78 per cent. (4.324 g. licorice gave a residue of 0.4229 g.).

Characteristic of this licorice was its extraordinary content of copper. Every solution in water, even of quite small quantities, showed in the insoluble sediment a more or less large quantity of pure copper, sometimes as a powder and sometimes in large, long, flaked pieces. I have found pieces as long as 5 millimeters, and weighing as much as 0.062 grams.

In the present research, this was the only kind of licorice used. The controls covered over 100 individual glycyrrhizin estimations, and consumed more than half a year. In order not to be affected by changes in humidity, which would naturally cause changes in the moisture content of the licorice, I used a finely powdered extract, which had been dried for several days in a vacuum desiccator over sulphuric acid, and of whose moisture content I could be assured. An experiment showed that 5.0358 g. of dried licorice after drying to constant weight at a 100°, lost 0.2652 g. The dried licorice which I used for all this work therefore still contained 5.27 per cent. moisture. In order to obtain comparative results I naturally followed exactly the methods described. If, for any reason, this could not be done, I made particular note of it. If an author's directions were ambiguous, or if they seemed to me to be missing at some important point, I substituted, particularly when it was a question of volumes of liquids, amounts which seemed to me suitable for the case in point. On repeating particular experiments, I was naturally guided by the amounts added previously, in order to be able to compare the values obtained. I always conducted two determinations side by side by the same method. The experiments were repeated until I obtained average values which did not differ from one another by

more than 0.5 to 0.6 per cent. In spite of the greatest care, and keeping experimental conditions as nearly alike as possible, it was difficult to obtain values which agreed well. Many other investigators with glycyrrhizin have made the same observation. All weighings were made on a chemical balance to within one-half mg. Liquids were evaporated on the water bath. Drying to constant weight took place in a water oven which always showed 98° C. I also used this oven when the directions called specifically for 100°, being convinced that the difference of 2° was of less importance than the advantage of always having a uniform temperature.

SUMMARY OF THE PUBLISHED METHODS FOR GLYCYRRHIZIN  
DETERMINATION.

- A. Extraction liquid: Water without the use of alcohol.  
Precipitation with sulphuric acid: (1) Rump, (2) Helfenberger, (3) Capin.  
Precipitation with hydrochloric: (4) French Pharmacopœia.
- B. Extraction liquid: Water with addition of alcohol.  
Precipitation with sulphuric acid: (5) Diehl, (6) Kremel, (7) Py, (8) Parry, (9) Evans' Sons, Leshner & Webb, (10) Houseman, (11) Erikson, (12) Guignard.  
Precipitation with hydrochloric: (13) Gadais I, (14) Gadais II.  
Precipitation with absolute alcohol: (15) Trubeck.
- C. Extraction liquid: Ammoniacal water without addition of alcohol.  
Precipitation with sulphuric acid: (16) Schröder, (17) Müntzer, (18) Morpurgo.  
Precipitation with hydrochloric: (19) Dutch Pharmacopœia.
- D. Extraction liquid: Ammoniacal water with addition of alcohol.  
Precipitation with sulphuric acid: (20) Kinzey, (21) Anselmino-Gilg.  
Precipitation with hydrochloric: (22) Stoeder, (23) Telle, (24) Durier.
- E. Extraction liquid: Alcohol-sulphuric acid.  
Precipitation with sulphuric acid: (25) Haffner, (26) Cederberg, (27) Schmidt (Haffner).

The control experiments which now follow are arranged in the order of this table.

1. *Rumpf (1855).*

"One part of licorice extract is dissolved in three parts of water. Half an ounce of the solution is diluted with one ounce of water, and one drachm of dilute sulphuric added. The washed and dried precipitate should amount to between five and seven grains."

Converted to our present system of weights, Rumpf would require that from a solution of 3.75 g. of licorice in 45 g. water, 0.3 to 0.42 g. glycyrrhizic acid should be separated by 3.75 g. dilute sulphuric acid. He therefore requires 8 to 11.2 per cent, a content which indeed corresponds approximately to present-day requirements. This method of Rumpf has, of course, only historical interest, as the first published glycyrrhizin estimation. I therefore did not attempt to check it up.

2. *Helfenberger Annalen (1897).*

"Five grams licorice extract are dissolved in 50 g. water, filtered, the filter washed with water, and 5 cc. dilute sulphuric acid added to the filtrate. The precipitate is collected on a small filter, washed well, dissolved in ammonia, filtered, the filtrate evaporated in a weighed dish, and the residue dried at 100° to constant weight."

A solution of 5 g. licorice in 50 g. water filters with great difficulty. I required in one case, eight hours to filter and wash that quantity until nearly colorless. The method in its description is so vague that one can obtain results which agree only when one completes the missing instructions. He says, "Filter, wash with water, and wash the precipitate thoroughly." These instructions, on account of their inexactness, must give large differences in the values obtained. To wash the insoluble residue, I used 50 cc. of water which, however, was not enough to obtain a completely colorless filtrate. To wash out the acid I used 30 cc. in small quantities. Dropping ammonia on the filter paper holding the acid, was not practical, as the liquid filters with great difficulty. As the instructions may also be interpreted I have dissolved the acid on the filter paper in warm ammonia, filtered, and washed the filter paper until colorless. From several experiments, I obtained between 6.9 per cent. and 7.2 per cent. yield, weighing 0.344, 0.348, 0.357, 0.360, 0.365 g. ammoniated glycyrrhizin from 5 g. licorice. From the method given in the introduction, I obtained as the loss from the 5 g. licorice 0.18-0.19 g. glycyrrhizic acid, corresponding to 3.6-3.8 per cent.

The high losses are caused by washing the precipitated acid with much water, and by the solubility of the acid in the supernatant liquid. I obtained 29 to 30 per cent. insoluble residue. Helfenberger's method does not attempt a purification of the precipitated acid. Since alcohol is not used to precipitate gums and other materials, the glycyrrhizic acid weighed is very impure.

Even in Helfenberger's "Annalen" of 1913, this method is used. It is surprising that it has not been improved in the course of years, since in latter years many practical proposals have been published.

### 3. *Capin (1911).*

"Two g. of licorice are dissolved in 20 cc. distilled water, the filtrate is transferred to an Erlenmeyer flask, 2 cc. sulphuric acid (66 per cent.) are added, and the vessel allowed to stand on ice with frequent shaking. After standing 24 hours, the liquid is poured on a smooth filter paper and the residue quickly washed by decantation with water at 0° to remove the last traces of sulphuric acid. The wash waters are passed through a second smooth filter, and the glycyrrhizic acid collected on this. Through the second filter is run 10-15 cc. distilled water containing 5 drops of ammonia to every 10 cc., and the liquid is received into the Erlenmeyer flask. The filter is washed with water, and the solution evaporated and weighed in a tared dish. The loss from 2 g. of licorice is reckoned as 0.11 and is added in."

This method uses the experience of a long research which I treated in detail, and aims to be an improvement of the method of the French Pharmacopœia. Although Capin's method may be regarded as an improvement, it contains a number of serious errors.

Two g. licorice are to be dissolved in 20 cc. of water, and the solution filtered. Capin uses no alcohol. This filtration requires a long time. From the filtrate, the glycyrrhizin is to be precipitated by sulphuric acid. Capin does not speak of washing the filter, although, of course, it should be obvious. If, however, one would wash until almost colorless, one would obtain a volume of more than 50 cc., from which to precipitate glycyrrhizic acid (in one case I used 35 cc. wash water, and in three other cases none at all, since the method does not call for it). If one omits the washing, losses result from the material staying on the filter. But if one does wash the filter, the quantity of acid precipitated is diminished because of

the greater solubility in the increased quantity of water. The supernatant liquid is poured off from the acid, and the latter washed free from sulphuric acid by decantation with water at 0°. The quantity of water to be thus used is not stated. From 2 g. licorice, I weighed 0.140, 0.151, 0.156, 0.160 g. ammonium glycyrrhizinate, that is 7-8 per cent. This amount would be increased to 12.7-13.5 per cent. by the improvements mentioned below.

These values are too low, more particularly because of the losses from the solution remaining on the filter. I found the loss from 4 g. of licorice to be 0.051 and 0.061 g. of glycyrrhizic acid, *i. e.*, 1.25-1.53 per cent. On the filter there remained 32 per cent. of insoluble matter. It can be seen from the above that this method has been badly worked out, and the necessary directions for obtaining accurate results are missing. This method can therefore give only unsatisfactory results. No purification is prescribed, and Capin does not use alcohol in spite of the great advantages obtainable thereby. The ammonium salt weighed is therefore very impure. Capin makes the very interesting experiment of decreasing the solubility error by adding a factor, good for every case, to the value obtained. In the introduction I have already pointed out that Capin obtained this solubility factor by shaking up an excess of glycyrrhizic acid with water and estimating the soluble part at 15° and 0°. He calculates the factor for 20 cc. of liquid precipitated and so obtained the number 0.110 to be added to the value found for ammoniated glycyrrhizin. This improvement is wholly undemonstrated and lacks any real basis. The following objection applies to it: The solutions used in glycyrrhizin determinations are never saturated, but are always quite weak. This is particularly the case with those solutions which are to be corrected for losses through washing.

[TRANSLATOR'S NOTE.—Here follows a half page more of further objections to Capin's method. (P. A. H.)]

*4. French Pharmacopœia (1908).*

"Two g. licorice are taken up in aqueous solution, filtered, made to 100 cc. and 30 drops of hydrochloric acid are added. After standing 24 hours, the liquid is poured through a filter, the residue and filter washed three times with 8 cc. portions of water, and then 10-15 cc. water, containing 5 drops of ammonia per 10 cc. is poured through this filter. The filter is washed with distilled water, and the solution of

ammoniated glycyrrhizin is evaporated to dryness on the water bath, and weighed. A weight of at least 0.2 g. is required."

This Pharmacopœia method does not state in how much water the licorice is to be dissolved. I always used 30 cc. and washed the insoluble residue until I had 100 cc. filtrate. The filtration took a long time. For the precipitation, 30 drops of official hydrochloric acid were used (Sp. Gr. 1.171, 22° Be.), which method I adopted. The filtration of the precipitated acid takes a very long time if a smooth filter is used. Therefore in the following experiments I always used a fluted filter. Three 8 cc. portions of water are not sufficient to wash the glycyrrhizin precipitate until colorless. There is, therefore, the possibility, that water-soluble materials which should be washed out, are later weighed as ammoniated glycyrrhizin. It is quite incomprehensible why the French Pharmacopœia specifies a solution of the glycyrrhizin salt in 100 cc., and precipitates the acid from this large volume of water. Twenty cc. of liquid would be quite sufficient. The use of such a large excess of water results in very appreciable losses. The precipitation takes place with hydrochloric acid, but the amount of acid prescribed is much too small, so that not all of the glycyrrhizin is precipitated, an observation which Capin himself made. If after adding the hydrochloric acid according to directions, the mixture is allowed to stand 24 hours and the glycyrrhizin filtered off, the filtrate shows a further precipitate on standing when additional hydrochloric or sulphuric acid is added.

[TRANSLATOR'S NOTE.—Other objections to this method are mentioned, including the fact that alcohol is not used. (P. A. H.)]

The values which I have found for the losses involved, prove sufficiently that the method of the new French Pharmacopœia is entirely useless. It is really quite remarkable that even in 1908 such a poor method could be adopted when a whole series of publications were available which would have given practical results.

##### 5. *Dichl* (1883).

"Ten g. licorice are digested, until disintegrated, with 10 cc. distilled water in a flask. After cooling, 200 cc. of alcohol are added, and allowed to stand several hours with frequent shaking. The liquid is then filtered through a double filter and the residue washed with a mixture of alcohol and water (2:1) until the filtrate is colorless. The alcoholic filtrate is evaporated to a syrup, dissolved in

water, and sulphuric acid added as long as a precipitate forms. The glycyrrhizin is washed with water, dried in the air and dissolved in strong alcohol. The alcoholic solution of the acid is filtered, the filter paper washed with alcohol, and the solution evaporated to dryness. The residue is dissolved in ammonia, and evaporated, dried, and weighed in a tared porcelain dish."

Diehl precipitates gummy and mucous substances with a large quantity of alcohol. The filtered and evaporated alcoholic extract is dissolved in water. The quantity is not stated, and further, the amount of sulphuric acid to be used for precipitation is not given. I also fail to find any statement as to how long the precipitate is to stand, and how much water is to be used for washing. In order not to obtain different results on account of these missing instructions, I supplied those which seemed to me to be suitable. I dissolved the evaporated extract in 60 cc. of water, precipitated with 5 cc. dilute sulphuric acid, and washed afterwards with 50 cc. water. Diehl now attempts a purification of the precipitated acid by re-dissolving in strong alcohol, previously drying the acid in air. If one takes freshly precipitated glycyrrhizic acid which is not quite dry, and treats it on a filter paper with absolute alcohol, one can wash the filter quite white, without any trouble, particularly if one warms the alcohol a little. If, however, one makes the precipitated acid quite air dry, perhaps even in a desiccator, it is then found that a part of the acid has become quite insoluble in alcohol. Since one can scarcely assume that glycyrrhizic acid, through simply standing a few hours in the air, or in a desiccator, would be decomposed, and since, further glycyrrhizic acid is soluble in hot absolute alcohol, one must regard the residue remaining on the filter as an impurity. An explanation for the different behavior of the moist and dry acid toward alcohol, is difficult to find unless one considers the possibility that the very small amount of water remaining on the filter in the first case dilutes the absolute alcohol, and so dissolves the glycyrrhizin. Such an influence, however, could only be effective for a few moments, since the absolute alcohol at once penetrates the filter. I must accept as the only possible explanation, the formation of a colloidal solution. In any case, I am of the opinion that this residue, which is insoluble in alcohol and easily soluble in ammonia represents impurities in the acid. Since such a purification is easy to carry out, its use in the quantitative determination is certainly to be recommended.

The insoluble residue on the filter, I dissolved in ammonia and evaporated in a weighed crucible. The weight varied between 0.09 to 0.11 g. There is therefore 0.9 to 1.1 per cent. weighed as ammoniated glycyrrhizin, which only consist of impurity in the acid. The ammoniated glycyrrhizin, obtained by Diehl's method is of a much lighter color than that from other methods. The difference is very noticeable. It is remarkable in this determination, that Diehl does not simply weigh the alcoholic solution of glycyrrhizic acid which he evaporates to dryness. Instead of that, he dissolves the dry residue again in ammonia, transfers to a tared dish, and weighs after drying again. This unnecessary, roundabout way results in much loss of time, and only renders errors possible. I obtained from 10 g. licorice 8.24-8.44 per cent. As losses, I obtained 1.91-2.11 per cent. The insoluble matter was 39-40 per cent. of the licorice taken.

The method of Diehl, in the form given, cannot be used on account of such vagueness. If, however, the missing instructions are intelligently completed, and one omits the useless conversion of the dried acid to the ammonium salt, one obtains good results, and a precipitated acid of a high degree of purity.

6. *Kremel (1899).*

"For the estimation of glycyrrhizin, 5 g. of roughly-broken licorice extract are dissolved in 50 cc. water, and allowed to stand several hours with frequent stirring. After disintegration, 50 cc. of 90 per cent. alcohol are added, stirred, the mixture allowed to settle, and filtered through a small fluted filter. The contents of the filter are thoroughly washed with 40 per cent. alcohol. The alcohol is evaporated from the filtrate on the water bath. After cooling, sulphuric acid is added to precipitate the glycyrrhizin. This is collected on a small filter, well washed with distilled water, and finally brought into solution by dropping ammonia on the filter. The ammoniated glycyrrhizin is collected in a dish, evaporated to dryness on a water bath, dried at 100° and weighed."

Kremel's method is inexact in some details, so that comparative values cannot be directly obtained from it. It is not stated how much alcohol is used to wash the insoluble matter. I found 50 cc. yielded a nearly colorless filtrate.

[TRANSLATOR'S NOTE.—Other sources of error due to vagueness are mentioned, including failure to specify quantity of sulphuric acid and of water used for washing the precipitate. (P. A. H.)]



The method discussed above which was published in 1889 has become the basis for a large number of methods published later. Although certain changes have been introduced in these later methods, the principle has remained the same. After intelligent completion of missing or faulty directions, the method gives practical results.

7. *Py* (1897).

"Two g. licorice are dissolved in about 30 cc. water on the water bath. After cooling, alcohol is added until a strength of 75 per cent. alcohol is attained. After standing 12 hours, the mixture is poured through a fluted filter, and the filter and residue washed with 75 per cent. alcohol. The alcohol is evaporated, the residue dried at a 100°, and weighed. It is then dissolved again in lukewarm water, and treated with dilute sulphuric acid (1:9). The precipitate is collected on the filter, and washed, first with water acidified with sulphuric acid, and then with distilled water, and finally dissolved from the filter with saturated ammonia-water. The filter is washed with ammonia until colorless. The ammoniacal solution is evaporated, dried at 100°, and weighed."

This method does not give detailed instructions, and further makes rather many inexact statements. Otherwise it does not differ from the others.

[TRANSLATOR'S NOTE.—The author (Linz) also objects to evaporating the alcoholic solution to dryness, also to the fact that *Py* does not state quantities for dissolving the dry alcoholic extract in water, for sulphuric acid used in precipitation, and for acidified water used in washing. In control experiments, Linz obtained 7.6-8.15 per cent. ammoniated glycyrrhizin with losses estimated at 2.22-2.75 per cent. The insoluble matter he determined as 47 per cent. (P. A. H.)]

This glycyrrhizin determination gives, therefore, the usual values if one intelligently completes the many inexact instructions. If one does not do this, one cannot obtain comparative results. The method in its original form cannot, therefore, be used.

8. *Parry* (1910).

"2.5 g. licorice are covered with 15 cc. hot water, and warmed on the water bath until dissolved. After cooling, 25 cc. 80 per cent. alcohol are added slowly with stirring and then 50 cc. 95 per cent.

alcohol. The liquid is allowed to stand half an hour, then filtered, and washed with 80 per cent. (by volume) alcohol until colorless. Filtrate and washings are evaporated to a syrup to remove the alcohol. The residue is transferred to a flask and made up to 30 cc. with water. Three cc. of dilute sulphuric acid (10 cc. of  $\text{H}_2\text{SO}_4$  plus 300 cc. water) are added slowly with stirring. After allowing to stand over night at  $12^\circ$ - $15^\circ$ , the liquid is decanted, and the precipitate washed four times with ice water, and dissolved in alcohol. To neutralize free sulphuric acid 2 drops of ammonia are added, and the solution evaporated on water bath to constant weight in a tared dish."

The method of Parry gives the usual picture of a glycyrrhizin determination. With a few changes this method has been adopted by Evans' Sons, Lesher & Webb, and by Houseman. The gums are precipitated with much alcohol, etc. The proportion, 2.5 g. of licorice to 15 cc. water, is in my opinion, the strongest solution which can be used without fear of loss. The addition of alcohol to give a mixture of 80 per cent. strength is presumably the strongest alcoholic solution which may be used. The good results obtained show that, by the experimental conditions given, losses do not result. The alcoholic solution after evaporation is taken up to 30 cc. In my opinion this volume is correctly chosen according to experience. The requirement to stand overnight at  $12^\circ$ - $15^\circ$  C. is probably not always called for. The supernatant liquid is to be poured off, and the acid is to be treated by washing and pouring off four times with ice water. I only succeeded twice in getting the glycyrrhizic acid to stick to the bottom so that it could be washed without loss. In such a case one must take a more roundabout way, collecting the acid on the filter and then dissolving it in hot alcohol. By this treatment losses are not excluded. Unfortunately Parry gives no quantities for washing with ice water, but it is highly necessary to prescribe exact quantities. The values received in checking the method are good. I obtained from 2.5 g. licorice, 0.230, 0.234, 0.239, 0.249, 0.249 g. glycyrrhizic acid, *i. e.*, 9.44-9.96 per cent. The losses on 5 g. licorice I determined in two experiments to be 0.0284-0.0314 g. glycyrrhizin, *i. e.*, 1.1-1.3 per cent. I found about 49.5 per cent. insoluble matter. In summarizing, I would state that the Parry method gives usable results, although a purification of the acid is not attempted.

*9. Evans' Sons, Leshner & Webb (1910).*

"2.5 g. of finely powdered material are weighed into a little beaker, 15 cc. water added, and warmed on the water bath to dissolve. After cooling, 23 cc. technical alcohol mixed with 2 cc. water, are added with stirring, and then 50 cc. alcohol. After standing for half an hour, the liquid is filtered into an evaporating dish and the precipitate is washed with a mixture of 50 cc. of technical alcohol with 4 cc. water. The filtrate and washings are evaporated to a syrup on the water bath, transferred to a thin-walled glass cylinder with 30 cc. water, cooled in melting ice and mixed with 3 cc. sulphuric acid (1-30). The contents of the cylinder are brought to freezing in an ice-salt mixture, and the glycyrrhizin is obtained as a solid mass on the bottom of the cylinder by allowing to thaw slowly. It is washed by decantation with 50 cc. water at 0°, and as much of the liquid decanted as possible. Two cc. ammonia water are then added, and the precipitate transferred to a weighed crucible with absolute alcohol, evaporated and dried at 100° to constant weight."

This method is founded on that of Parry. The numbers, quantities and strength of alcohol agree exactly. The only new thing is the attempt to use the fact that glycyrrhizic acid is more difficultly soluble in water at 0° than in water at room temperature. Against the practicability of this idea, which is good in itself, I have objections which I will hereafter explain. This method was only available to me in a translation (*Jahresbericht der Pharmazie*, 1910, p. 239). As I did not understand the expression "Technical alcohol" in the translation, I requested information from the Editor of the "Chemist and Druggist." I then learned that "technical alcohol" (Industrial methylated spirits) has the same significance as our "vergällten spiritus." This spirit is denatured with wood naphtha, which corresponds to our pyridin bases, in the proportion of 19:1. I considered that I might dispense with the use of denatured alcohol in my check experiments since its use is only explainable by the fact that pure alcohol is so extremely expensive in England. The mixtures describing this method, as regards strength of alcohol, are exactly the same as Parry's, so that my remarks on the latter apply. In my opinion, one-half hour's standing is not enough to precipitate all the starch and gums. At any rate, in a control experiment it was found that after standing and filtering according to directions there formed after a few hours a further light precipitate, which could only consist

of gums not previously precipitated. These gums could possibly have been weighed finally as glycyrrhizic acid. The filtrate is then to be evaporated to a syrup, and transferred with 30 cc. water to a thin-walled glass cylinder. I used a wide test tube for this purpose.

[TRANSLATOR'S NOTE.—Linz goes on to show that the proposal of Evans to obtain the glycyrrhizin sticking to the bottom of the vessel by freezing and subsequent thawing is a good idea, but unfortunately does not work out in practice as described. Linz tried it six times unsuccessfully. (P. A. H.)]

(To be Continued.)

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## PLANT COLORS

By DR. HENRY KRAEMER, Mt. Clemens, Mich.

The nature of plant color has been the subject of some investigation and considerable speculation. There is no objection to constructing theories concerning the origin, nature and functions of plant colors, providing we recognize that they are apt to be, with our meager knowledge of plant color substances, mere speculations, and it is doubtful if any of our theories will stand the test of time as new investigations are made. There are probably a few facts that we recognize, and some of these may be briefly stated as follows:

1. The name anthocyanin as first given by Marquardt may be used to designate all the plant colors, other than the green and yellow which are plastid colors. The anthocyanin colors usually occur in the cell sap and may be present in flowers fruits, roots and leaves of higher plants, or even in the lower plants.

2. In the marine algæ the anthocyanin colors seem to be contained in plastids and are usually not liberated and distributed free in the cell until the death of the filament. In the higher plants the anthocyanin colors are usually present in the vacuoles of the cell and are usually of either a blue or red color, but many intervening shades of red and blue are to be seen.

3. The blue anthocyanin are variously distinguished, some being quite permanent as in the flowers of *Delphinium*, *Viola* and *Malva*, even on the death of the cell or drying of the plant, whereas in other plants they are decomposed, changing to a fawn or brown color, as in the flowers of *Pawlonia*, *Bellis*, etc.

4. The blue anthocyanin colors may separate under certain conditions as when there are marked changes in temperature or other disturbances in the cell in the form of either spherical globules, which may be relatively numerous as in the petals of *Catalpa* or in larger globules as in the petals of *Cineraria*, *Delphinium* and blue hydrangeas, or may show a spherite structure or separate in the form of long rods as in the leaves of red cabbage.

5. The red anthocyanin colors are of two kinds:

- a. Those which change to a blue or purplish red as in the rose, *mertensia*, tiger lily, tulip, *cineraria*, dogwood, red hydrangea, and red cabbage.
- b. Second class includes those red anthocyanins which do not change in color as in red apples and in nearly all of the red fruits.

6. Anthocyanin colors may also occur in the same cells which contain either chloroplastids or chromoplastids. As examples in which both chloroplastids and anthocyanins occur in the same cell may be mentioned the leaves of wild carrot, the beet, and purple beech. Chromoplastids and anthocyanin colors are frequently to be found in flowers as the nasturtium and tiger lily.

7. Anthocyanin colors while found in the stems and leaves, and also in thorns as in roses are usually more pronounced or more strongly developed in those organs at the extremity of the plant or at the tips or shoots as in the purple beech and in flowers generally.

8. Plant color substances from their solubility may be grouped into two classes:

- a. Those while like the plastid color substances are insoluble in water and soluble in immiscible solvents as petroleum benzine, toluol, ether, etc.
- b. Those which are soluble in water or at least in hydro-alcoholic solutions, but insoluble in the immiscible solvents.

9. The investigations of plant color substances show that they may be brought into probably three groups:

- a. Colorless, or leuco-compounds, which upon oxidation form distinct color substances as in the lichens.

- b. Glucosides, which on the action of ferments yield color substances as those forming the yellow pigment, quercetin.
- c. Substances which possess a basic radical or chromophore, and which manifest distinctive colors depending upon the arrangement of certain groups and side chains. There is a disposition by some authors to consider that the shades of color are due to an enzymic action on the chromatin. It is not easy to refute this latter claim as enzymes are always present in the plant cell, and it is not always easy to dissociate the action of the enzymes from that of other substances which are capable of producing equal changes in the color of a pigment. That there are very many substances capable of producing color changes in plant pigments is well known, but unfortunately these changes are not due in the plant cell to the replacement of the hydrogen ion with some basic radical. A microscopical study of plant organs containing anthocyanin colors usually show in the different cells varying reactions which, while they might be ascribed as being due to enzymes, are more likely to be the result of the interaction with other substances.

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## SOME EXPERIMENTS ON THE MODIFICATION OF COLOR IN PLANTS.

By DR. HENRY KRAEMER, Mt. Clemens, Mich.

The study of color in plants may be pursued in several directions: 1. They may be biological or functional. 2. They may be chemical or constitutional. 3. Or they may be physiological or cellular. Studies involving any experiments with the view of modifying color in plants are fundamental studies connected with the physiology of the plant cell.

Probably the most fundamental studies are those which are of a chemical nature in which the constitution of color compounds is

demonstrated. On the other hand, such studies are quite difficult, and usually will involve considerable expense, as large quantities of material are necessary in order to obtain a given constituent. It is my object in this paper to report on some experiments which I conducted nearly ten years ago with a view of modifying color in flowers. These studies have not been previously reported upon, because the results at that time did not seem to be sufficiently strongly marked, and unless the paper was illustrated with colored plates, no adequate idea of these changes could be seen. Fortunately all of the work which I did at that time is conserved either with colored photographs or with drawings in which the shades of color were quite accurate. Upon resuming my work in the study of color in flowers I have become impressed with the fact that this earlier work was really more valuable than I thought, at the time.

Studies of changes of the color in flowers, the plant being in a fixed environment is essentially a physiological study of the plant soil.

Upon the sea coast the flowers of the *Hydrangea Otaksa* invariably become blue in the second year even though the flowers in the plants were pink or a strong reddish color. This is usually attributed to the salt air, the fine spray of sodium chloride having an influence on the color change. The older, weakly woody plants of *Hydrangea Otaksa* almost invariably have a tendency to produce blue flowers, although in many environments the plants will run into foliage and not produce any flowers at all. It is a very common belief that the flowers of hydrangea may be changed by the introduction of chemicals into the soil. In fact, very many gardeners who are anxious to have blue flowering hydrangea plants at Easter time, invariably add a piece of alum about the size of a walnut to the soil of the pots during the summer. The study of the pigment cells of any portion of the plant shows that the change of color would be produced by a great variety of reagents. It is quite well known that the substances of the soil may be changed by the introduction of chemicals or other soils. These produce changes in the plant cell. The carbohydrates for instance in a green algæ may be changed into reserve starch by adding calcium nitrate to the water surrounding them. In the same way a reserve starch will be duplicated in the cells of foliage leaves when they are attacked by certain fungi.

The colored areas of the plant are generally located at the terminal portions and are usually located in the tissues in the periphery of these organs. It is quite likely and seems very reasonable that if the proper chemicals were supplied the plant in an unaltered form or if they could be supplied in such a form that they would be altered by the cell distinct color changes would ensue. In other words the same change would be attained as we find on treating the pigment cells upon a slide with reagents or substances which are usually present in the soil and water. It is quite possible that studies on the algae would yield some striking and variable results in this particular. The great difficulty would be in noting this change in color, which, however, could be followed by the device which I have made for use in the study of color in higher plants. Again, before taking up flower color substances this work might be developed in the study of color in root-like organs, in the raddish.

In my own experiments I think the mistake that was made was in not studying more extensively the distribution of colors in flowers than I did. Subsequent studies show that the pigment is distributed in four ways in the flower: 1. The pigments are usually in epidermal cells as in the rose and pansy. 2. The pigment may occur in sub-epidermal cells in addition as in wild hyacinth. 3. It may occur in the mesophyl layers in addition as in *Mertensia*. 4. It may occur in the conducting tissues surrounding the mestome strands in the flower as in blue hyacinth. From this study of the distribution of flower color substances it would seem that if the study was made of those plants in which the pigment in the flowers was in the immediate proximity of the fibro-vascular bundles that the chemical supplied the plant through the soil might be more or less unaltered and produce communication in the pigment cells.

Of course, there are a number of other features that are fundamentally important and that should be ascertained only at the time of formation of flower coloring process. It would appear that these are usually formed some time after the organs of the flower have been formed. However, in the foliage of very many plants that produce flowers there are indications that the pigment is formed in the early stages of organs in which photosynthesis takes place, as in the rose. In fact, the pigment in the foliage of the rose as well as in the prickels closely correspond to the pigment of the flowers.



## STUDIES IN EXTRACTION.

By JAMES F. COUCH.

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### I. THE RATE OF EXTRACTION OF PHYTOLACCA DECANDRA.

In a general survey of the theory of percolation<sup>1</sup> I have pointed out the desirability of more data on the rates of extraction of various drugs to fill in certain gaps in our knowledge of percolation. The rate of extraction may be determined in several ways: In this paper and in two which are in course of preparation, three methods have been employed which differ only in extensiveness. Data already published on the rates of extraction may be found in the published works of Lloyd, Squibb, McIntyre and Robbins, reference to which may be found in above quoted survey.

The previous work on this subject, however, was carried out at the time when the standard for fluidextracts was a grain per minim instead of a gram per millilitre as at present, and the modern fluid-extract is but 95.14 per cent. of the strength of that of forty years ago. As the earlier work was conducted with reference to the former standard it is highly desirable that it should be reviewed with respect to the present standard for the sake of exactness and completeness. In addition, the earlier work was conducted particularly so solve questions of economy of menstruum, of time, or in attempts to avoid evaporation of weak percolates.

The following account presents the results of an inquiry into the factors which govern the rate of extraction of phytolacca, the generalizations which underlie it, and the conditions which obtain. The theory of the process has already been discussed.<sup>2</sup>

It was found that the extraction of phytolacca proceeds in a regular manner, but with diminishing velocity, so that the last portions of extractive require a considerable volume of menstruum for their removal. This is in conformity with the published results of all previous investigators which bear at all on the subject. There appears to be a point where the cellulose of the drug exerts an attraction for the extractive equal to that of the menstruum for the extractive. At this point equilibrium will be established and the

<sup>1</sup> This *Journal*, Vol. 92, Nos. 11 and 12 (1920).

<sup>2</sup> This *Journal*, Vol. 92, p. 788, *seq.* (1920).

velocity of the extraction will become zero. The extraction of phytolacca is extremely rapid at the beginning of the process, and when a volume of percolate thrice the amount of the fluidextract equivalent to the weight of the drug had been collected, 97 per cent. of the total extracted matter had been dissolved out of the drug. In other words, the percolation of one gram with three millilitres of menstruum removed 97 per cent. of the total extract obtained.

In accordance with this assumption that the attraction of the marc is one of the factors which govern the rate of extraction of a drug a number of mathematical formulas were applied for the purpose of calculating a constant distribution ratio between menstruum and marc. The results in all cases showed a progressive variation, either a numerical increase or a decrease and no constant was obtained. (Fig. I.) Other factors intervene, and these are probably the same as those which affect the velocity constant discussed below.

The results obtained in the actual extraction are plotted in Fig. II, where the ordinates represent grams per 100 ml. (additive), and the abscissæ gallons of percolate. This curve shows the regularity of the extraction, the rapid initial extraction, and the retardation which sets in later in the process. It may, with profit be compared with the plotted results of an extraction of cinicifuga reported by Lloyd,<sup>3</sup> which shows the same general characters. It will be noted that the cinicifuga was extracted much more rapidly than in phytolacca. Lloyd used 7680 grains of drug and 97 per cent. of the total extract was contained in the first 21 floz. of percolate. In order to duplicate that rate the present extraction would have to show 97 per cent. in the first six and one-half gallons, or about twice the true rate of extraction. The cinicifuga yielded about 5 per cent. and the phytolacca 32.75 per cent. of extract; consequently the difference in rate of extraction was not due to the amount of soluble matter in the drugs, but rather to a difference in solubility. It is thus apparent that phytolacca is more easily extracted than cinicifuga.

In attempting to apply a mathematical treatment to the rate of extraction it was decided that, since we have no quantitative knowledge of the various constituents of phytolacca, the quantity of extract should be dealt with as a unit. A number of formulas were applied, but all of them gave a series of results which exhibited the

<sup>3</sup> This *Journal*, 59/434 (1878). The results are plotted in this *Journal*, Vol. 92, p. 857 (1920).

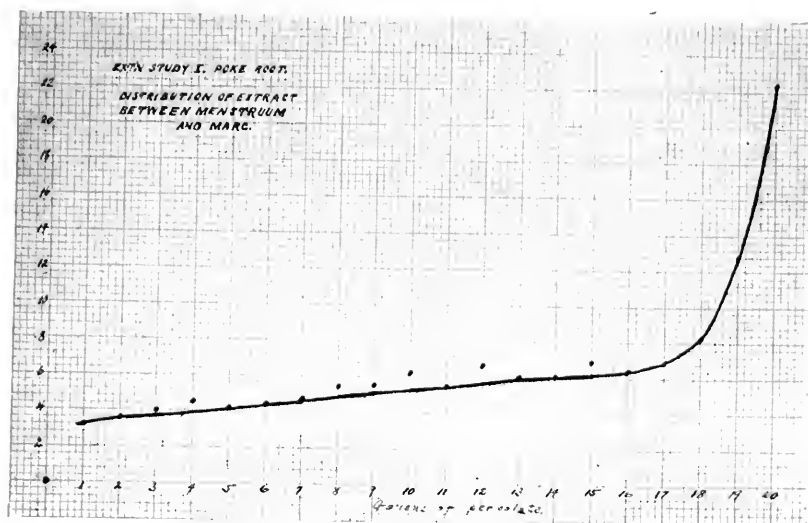


FIGURE 1.

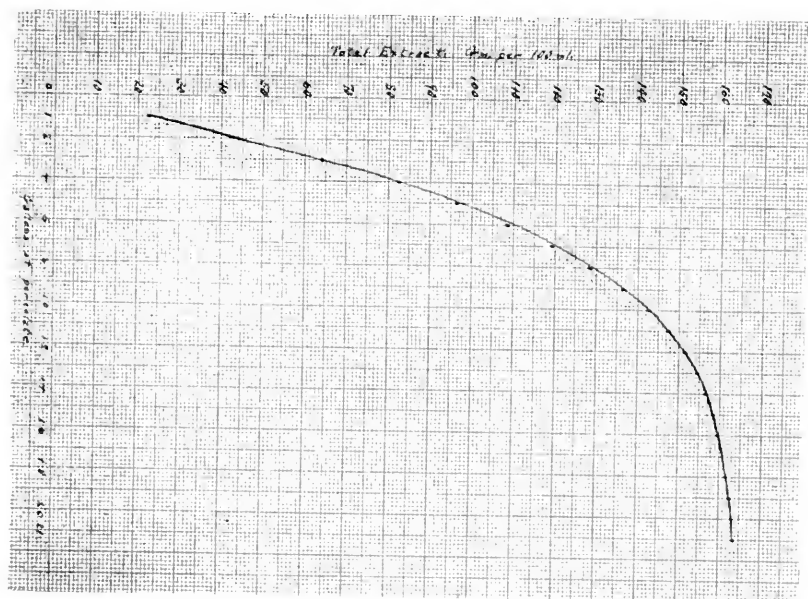


FIGURE 2.



same numerical increases or decreases observed in the attempt to calculate a distribution ratio. The factors applied in these formulas were functions of the concentration of extracted matter, undissolved extractive (this included that in the marc, that dissolved in the absorbed menstruum, and that dissolved in the percolate) and time. The lack of constancy in the results indicates that there are other factors which influence the rate of extraction, and we may here consider two: (1) Variation in the composition of the extract;<sup>4</sup> the more soluble matters are extracted first, leaving the more refractory substances to the less saturated portions of the menstruum; and (2) variation in the alcoholic strength of the menstruum,<sup>5</sup> with a consequent change in its solvent powers. The observed difference in alcoholic strength between the first and the twentieth gallons of percolate in this extraction was over 7 per cent. The first few gallons were diluted by the natural moisture of the poke root, which amounted to three or four pints, a quantity capable of seriously altering the solvent power of the menstruum. The fact that the alcoholic strength of the menstruum increases would lead to an assumption that the solvent powers of the menstruum increase as percolation proceeds and it is possible that, as the drug becomes more difficult to extract, the menstruum becomes more able to dissolve the extractive, but not proportionally. The two factors will thus tend to neutralize one another. With our present knowledge, however, it does not seem possible to characterize the rate of extraction of any drug by a factor which will represent conditions at any point in a percolation.

#### EXPERIMENTAL.

A quantity of *phytolacca* was purchased on the open market, identified, and ground to a coarse powder; 19,876 Gm. of this drug were percolated according to the directions of the U. S. P. 8. The drug was mixed with five gallons of diluted alcohol in a mechanical mixer, and the whole was packed firmly in a galvanized iron percolator of about twenty-five gallons capacity. This particular weight of drug was chosen so that the experiment might furnish somewhat more than five gallons of fluidextract of official strength.

The percolator was set in place, enough menstruum was added to displace the air and leave a stratum above the drug. The appara-

<sup>4</sup> Cf. Squibb, this *Journal*, 38/109 (1866); 39/402 (1867); 40/1 (1868).

<sup>5</sup> Cf. Lloyd, *Proc. A. Ph. A.*, 1881/408; 1882/508.

tus was then tightly closed and was allowed to macerate exactly 48 hours when percolation was commenced. The flow of percolate was so adjusted,<sup>6</sup> that one gallon of percolate was obtained in about one hour and one-half. The percolation was discontinued at 5.30 P. M., and was recommenced at 8 A. M. the following day. The procedure followed in collecting the samples was this: Each gallon of percolate was collected separately in a clean bottle connected by a rubber tube with the percolator to avoid contact with the air. The whole gallon was thoroughly mixed and a portion was then taken for analysis.

During the process the temperature of the percolator varied from 23° to 26° C. Fresh menstruum was added continually to replace that percolated out.

The specific gravity of the samples was determined on a Westphall balance standardized against water at 0° C. Alcohol was determined in a few samples by distillation of 50 ml. samples, dilution of the distillate to 100 ml. and determination of the alcoholic content from the specific gravity at 15.6° C.

The extract was determined by the following procedure: 25 ml. of the percolate were pipetted off into a weighed evaporating dish; the pipette was rinsed with 10 ml. of distilled water and the rinsings were added to the sample. This was then evaporated to constant weight on a water bath and was then heated to nearly constant weight in an oven at 105° C. The weight of extract so obtained multiplied by four gave the extract per 100 ml. Of course, volatile oils were driven off and lost. Check determinations of this method showed it to be accurate within 0.5 per cent.

The data obtained by the analyses and some of the calculations are recorded in Table I.

TABLE I, PART I.

Date.	Time.	Sample.	S.G.	<i>Extract.</i>		<i>Alcohol</i> <i>by Vol.</i>
				<i>Per 100 ml.</i> ( <i>E.</i> )	<i>Per Gallon.</i>	
June 17.	9.25 A. M.	1	1.0448	22.40 Gm.	848. Gm.	31.65%
" "	11.15 "	2	1.0415	21.60	817.7	
" "	1.10 P. M.	3	1.0355	20.12	761.6	
" "	2.45 "	4	1.0261	18.38	695.8	
" "	3.55 "	5	1.0157	14.04	531.5	32.5

<sup>6</sup> Cf. Discussion, this *Journal*, Vol. 92, p. 854 (1920).

Date.	Time.	Sample.	S.G.	Extract.		Alcohol by Vol.
				Per 100 ml. (E.)	Per Gallon.	
June 17.	4.55	"	6	1.0023	12.16	
" "	5.40	"	7	0.9946	10.58	
" 18.	8.25 A. M.	8	0.9861	9.56	361.9	33.7
" "	9.50	"	9	0.9800	7.42	
" "	10.55	"	10	0.9689	6.54	37.5
" "	11.55	"	11	0.9648	4.68	
" "	1.15 P. M.	12	0.9668	4.12	156.	
" "	2.15	"	13	0.9582	2.82	
" "	3.20	"	14	0.9558	2.20	38.3
" "	4.10	"	15	0.9546	1.84	
" "	5.00	"	16	0.9528	1.30	
" 19.	8.20 A. M.	17	0.9514	1.04	39.4	38.16
" "	9.15	"	18	0.9474	0.88	
" "	10.15	"	19	0.9465	0.82	
" "	11.25	"	20	0.9460	25.7	38.68
" 21.	Noon.	21	0.9489	0.60		

TABLE 1, PART 2.

Total Extracted Per 100 ml.	Extract Left in Drug (500 Gm.) (D.)	E/D.	<i>t</i> log E. D.	% Un- extracted.	% of Residue Extracted.
22.40 Gm.	141.38 Gm.	0.1621	0.1239	90.38%	90.38%
44.00	119.38	0.1803	0.1526	80.19	88.73
64.12	99.66	0.2018	0.1653	69.87	87.13
82.50	81.28	0.2261	0.1745	59.57	85.26
96.54	67.24	0.2088	0.1780	50.87	85.41
108.70	55.08	0.2207	0.1816	43.01	84.53
119.28	44.50	0.2377	0.1861	35.69	82.96
128.84	34.94	0.2736	0.1931	28.74	80.54
136.26	27.52	0.2759	0.1982	23.10	80.38
142.80	20.98	0.3117	0.2054	17.93	77.63
147.48	16.30	0.2871	0.2097	14.12	78.72
151.60	12.18	0.3382	0.2166	8.97	63.56
154.42	9.36	0.3012	0.2202	8.26	92.17
156.62	7.16	0.3072	0.2235	6.36	76.90
158.46	5.32	0.3466	0.2284	4.61	75.88
159.76	4.02	0.3233	0.2317	3.60	74.69
160.80	2.98	0.3489	0.2357	2.67	74.35
161.68	2.10	0.4190	0.2480	1.89	70.65
162.50	1.28	0.6406	0.2659	1.15	61.10
163.18	0.60	1.1231	0.2804	0.54	46.79
163.78					

On June 21st, after the drug had macerated for 48 hours, the twenty-first sample was collected. The analysis of this showed the drug to be pharmaceutically exhausted.

The finished fluidextract yielded the following data: Alcohol, 37 per cent.; extract, 32.54 Gm. per 100 ml.; S. G. 1.0371.

#### SUMMARY.

1. The extraction of the root of *Phytolacca decandra* proceeds regularly with diminishing velocity.
2. The rate of extraction is proportional to the total extract, inversely proportional to the residual extractive, the time, and an unknown factor or combination of factors. On account of these unknown factors a number characteristic of the extractibility of the drug cannot be assigned it.
3. It is probable that the unknown factors depend upon a change in the composition of the extract and a rise in the alcoholic content of the percolate.
4. The first fifteen gallons of percolate contained 97 per cent. of the total matter extracted.
5. It is shown that the alcoholic content of the percolate increases as the percolation proceeds. This has not hitherto been demonstrated.

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#### THE ASSAY OF ACONITE.

By DR. A. R. L. DOHME,

*Chairman, Committee on Aconite of Scientific Section of American Drug Manufacturers' Association.*

The work covered by this paper represents what has been done during the past three years by the Scientific Section of the American Drug Manufacturers' Association, who have felt that its results should be made known to the medical and pharmaceutical professions generally.

The primary problem was to attempt to decide whether the chemical assay of aconite and its preparations had any real value, and the resultant problem was to determine if the physiological assay was accurate and trustworthy. The present official assay process U. S. P. IX Revision is a chemical one with an alternative physiological assay, but the chemical assay is the standard. In the VIII Revision there was only a chemical assay as the official process. In



both cases the end product was represented by ether soluble alkaloids. We have shown that the ether soluble alkaloids are not all aconitine, but represent a more or less variable proportion of aconitine and its products of hydrolysis benzoyl-aconine and aconine. This variability alone makes the assay process of little value as an absolute standard of therapeutic efficiency and as well makes its relative or comparative value more or less of an uncertain quantity.

In order to determine definitely if the three alkaloids which constitute the ether soluble alkaloids—aconitine, benzoyl-aconine and aconine could be separated from one another by chemical means a supply of pure aconitine was procured and hydrolized into benzoyl-aconine and some of the latter hydrolized further into aconine. After thus converting a number of grammes in this way and obtaining a quantity of each of benzoyl-aconine and aconine in pure condition, attempts were made to determine if varying solubility in all available solvents or precipitation by all known precipitants might give a method of separating them when contained in a mixture. The result, however, was that no method was discovered by which they could be quantitatively separated, as they showed similar solubilities and precipitation by precipitants. It was, therefore, decided that a chemical separation quantitatively was not feasible and that, therefore, the so-called chemical method of assay was not possible, provided our aim was to get as the end-product of our assay only aconitine.

It was also determined by animal experiments that benzoyl-aconine and aconine do not possess the therapeutic properties of aconitine and their lethal dose was quite far removed from that of aconitine.

Hence the final conclusion reached was that the present chemical assay of aconite for ether soluble alkaloids was misleading and untrustworthy and had better be abandoned.

The next part of our problem was to see if a physiological assay could be developed which would be of some real value in determining approximately correctly the therapeutic efficiency of aconite and its preparations. This, of course, at once opens up the question as to the correctness of a method of assay which has as its criterion and basis the lethal dose or the amount that will kill a definite weight of animal per gram. Or in simple form is lethal power a basis for therapeutic efficiency, and is one drug that will kill 300 gm. of guinea pig in a dose of one milligram twice as efficient therapeutically upon

human beings as one that will kill 300 gm. of guinea pig in a dose of two milligrams. On this question pharmacologists and physiologists are apt to divide and differ. As lethal dose is the basis used in physiological assay methods, it is probably the only, and hence the best basis available for determining relative therapeutic efficiency of the drug.

Beginning with the pure aconitine crystals we used for making our hydrolysis products for above experiments our committee sent out samples of same and of a sample of fluidextract aconite to the physiological chemists of five different laboratories. The prime purpose of this was to determine whether results by such a minimum lethal dose method would be sufficiently close in the hands of varying laboratories and observers to warrant hoping to utilize it in an assay method—assuming, of course, that minimum lethal dose on guinea pigs would be a basis for therapeutic value. The results follow:

	<i>Aconitine cryst.</i> <i>gm. per gm. wt.</i> <i>of guinea pig.</i>	<i>F. E. Aconite Rt.</i>
Sharp & Dohme . . . . .	.0000000625	0.000300
Upjohn . . . . .	.0000000600	0.000266
Parke Davis & Co. . . . .	.0000000600	0.000300
Eli Lilly & Co. . . . .	.0000000625	0.000275
Norwich Pharmacal Co., . . . . .	.0000000510	0.000360

If we assume that minimum lethal dose on guinea pigs is a basis for therapeutic efficiency of aconite, then these results distinctly indicate that this method is sufficiently trustworthy and efficient to serve as an assay method to determine the therapeutic efficiency of aconite preparations based upon pure aconitine crystallized as a standard.

The Scientific Section of the American Drug Manufacturers' Association hence recommend that the chemical assay be dropped for aconite and its preparations and a physiological assay based upon aconitine crystallized U. S. P. be substituted in its place.

In my laboratory the m. l. d. for benzoyl-aconine and aconine were also determined on guinea pigs in comparison with the aconitine and the following results obtained:

*M. L. D. Guinea Pig.*

Aconitine cryst. . . . .	0.0000000625	gm. per gm. wt. of guinea pig.
Benzoyl-aconine . . . . .	0.00002	gm. per gm. wt. of guinea pig.
Aconine . . . . .	0.00025	gm. per gm. wt. of guinea pig.
F. E. Aconite Root . . . . .	0.00003	gm. per gm. wt. of guinea pig.

These results indicate that aconitine is about 300 times as efficient, *i. e.*, toxic as benzoyl-aconine, and 4000 times as toxic as aconine, and at the same time they apparently possess practically none of the characteristic properties therapeutically of the aconitine—as for instance, producing numbness on the tip of the tongue, etc.

The method employed in these experiments was for the Fluidextract Aconite to dilute 1 c. c. thereof to 10 c. c. with 50 per cent. alcohol. Use 300 to 400 gm. guinea pig and calculate the dose per pig and dilute this with normal salt solution to a total volume of 1.5 c. c. per pig. Inject this into the subcutaneous tissues of the abdomen and take as a lethal dose the smallest amount which will kill within 24 hours.

For the Aconitine—dissolve 0.1 gm. in 100 c. c. of 2 per cent. acetic acid. Dilute 1 c. c. of this solution to 10 c. c. with distilled water, giving a 1 : 10000 solution of aconitine. Calculate the total dose required for a pig of 300 to 400 gm. and dilute with normal saline solution to a sum total of 1.5 c. c. and inject as for the Fluidextract Aconite. Approximately 0.00000005 per gram is usually the lethal dose.

With the aconitine cryst. above used as a standard it will now remain to establish by comparative tests in various laboratories the extent of agreement reached in the application of above method of physiological assay for fluidextract and tincture aconite as well as the drug aconite, which latter will of course only be an application of the method of the two fluid preparations, as a liquid extract will have to be prepared to make the assay. This work is now before our Committee on Aconite and will doubtless be worked out some time soon.

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## PODOPHYLLUM ASH STANDARDS.

By E. L. NEWCOMB, C. H. ROGERS AND C. W. FOLKSTAD,

MINNEAPOLIS, MINN.

The present criticism of the 3 per cent. ash limit for *Podophyllum* appears to be well-founded. Much of the drug on the market at the present time has been carelessly cleaned and should no doubt be rejected or properly cleaned before being used. On the other hand, some very well cleaned samples yield considerably more than the permitted 3 per cent. ash.

The results of our studies show that there is considerable variation in the proportionate amount of roots and rhizomes, that these parts are sometimes plump and sometimes shriveled. Plump starchy roots and rhizomes contain a proportionately small amount of calcium oxalate and yield a low ash. Shriveled roots and rhizomes contain less starch, proportionately more calcium oxalate and yield a high normal ash. Some commercial lots of the drug consist almost entirely of plump or bold roots and rhizomes. Others represent a mixture, while still other lots consist chiefly of shriveled roots and rhizomes.

An excess of inorganic foreign matter has no doubt been responsible for much of the difficulty with the ash standard. The factors above mentioned, however, play an important part not only in the ash yield, but also in the resin yield. In addition many samples contain an excess of organic foreign matter. There is real need for a purity rubric to provide for more uniform drug. The following results should be helpful in determining the standards to be adopted. The ash tests have been run by Mr. C. W. Folkstad, under the direction of Prof. C. H. Rogers.

ASH AND PURITY OF SAMPLES OF *PODOPHYLLUM*.

<i>Sample No.</i>	<i>Description.</i>	<i>% To- tal Ash.</i>	<i>% HCl. Insol. Ash.</i>
No. 1.	Prepared from carefully garbled commercial drug, bought 1920, powd. this Laby. 1920 .....	2.51 2.64	0.34 0.21
No. 2.	Commercial sample powdered, bought prior to 1916 .....	3.35 3.19	0.30 0.34
No. 3.	Commercial sample powdered, bought about 1916 .....	4.08 4.08	1.07 1.10
No. 4.	Commercial sample coarse powdered, from stock .....	3.34 3.32	0.51
No. 5.	Commercial powder, bought 1911, in carton labeled "No. 40 powder" ....	4.60 4.55	1.32 1.23
No. 6.	Commercial powder, bought 1921, in carton, labeled "ash 4.40 per cent." ..	4.88 4.86	0.90 0.86

<i>Sample No.</i>	<i>Description.</i>	<i>% Total Ash.</i>	<i>% HCl. Insol. Ash.</i>
No. 7.	Commercial powder, bought 1921, in paper bag, labeled "Podophyllum U. S. P. Mandrake Powdered, Analyzed and Guaranteed".....	8.88 8.23	5.95 4.96
No. 8.	Sample prepared from 2-pound lot of whole podophyllum, bought in 1921, average portion powdered in this laboratory, 3-16-21. Not garbled ...	5.27 4.74	1.36 0.96
No. 9.	Sample prepared from average portion of 2-pound lot of drug bought 1921, powdered in this laboratory, 3-16-21. Not garbled .....	2.47 2.40	0.24 0.21
No. 10.	Sample prepared from 2-pound lot, bought 1921, average portion powdered in this laboratory, 3-16-21. Not garbled .....	3.73 3.66	0.66 0.55
No. 11.	Sample prepared from rhizomes only, mostly shriveled, very little soil, rhizomes separated from drug bought 1921, powdered in this Laby. Rhizomes represented 86.9 per cent. of the drug. Garblings 0.8 per cent. ...	4.67 4.35	0.89 0.64
No. 12.	Sample prepared from roots only, mostly shriveled, very little soil, drug same as No. 11, bought 1921, roots represented 12.2 per cent. of total weight, powdered in this laboratory, 3-24-21 .....	7.28 7.01	0.37 0.38
No. 13.	Sample prepared from rhizomes only, mostly plump, clean looking, drug bought 1921, rhizomes represented 89.1 per cent. of total weight, garblings 1.97 per cent. Rhizomes powdered in this laboratory, 3-24-21 ..	2.58 2.77	0.25 0.25

<i>Sample No.</i>	<i>Description.</i>	<i>% To- tal Ash.</i>	<i>% HCl. Insol. Ash.</i>
No. 14.	Sample prepared from plump rhizomes only, clean looking, drug bought 1921. Rhizomes hand brushed and powdered in this Laby. 3-24-21 . . . .	1.69 1.63	0.21 0.18
No. 15.	Sample prepared from roots only, plump, clean looking drug bought 1921. Powdered in this Laby. Roots represented 9.11 per cent. of the total weight . . . . .	3.69 3.96	0.87
No. 16.	Sample prepared from rhizomes only, some shriveled, some plump, drug bought 1921. Rhizomes represented 75.91 per cent. of total weight, garblings 6.97 per cent., rhizomes fairly clean looking, powdered in this Laby.,	3.93 3.91	0.96 0.93
No. 17.	Sample prepared from shriveled rhizomes only same lot of drug as No. 16, powdered in this Laby. . . . .	5.09 5.10	0.66 0.99
No. 18.	Sample prepared from roots only, some shriveled, same lot of drug as No. 16. Roots represented 16.4 per cent. of total weight, powdered in this Laby. . . . .	4.83 4.81	1.71 1.83

*Department of Pharmacognosy,  
University of Minnesota.*



GOLD MEDAL PRESENTED TO DR. FREDERICK B. POWER, PH. D., LL. D.



DR. FREDERICK K. B. POWER.



## PRESENTATION OF MEDAL TO DR. FREDERICK B. POWER.

On Monday, May 9, 1921, in the Auditorium of the Cosmos Club, Washington, D. C., a very interesting event occurred when Mr. Henry S. Wellcome presented to Dr. Frederick B. Power a gold medal in recognition of his services as Director of the Wellcome Research Laboratories for a period of nearly twenty years prior to 1914.

Dr. David Fairchild opened the meeting by reading letters from the following gentlemen, expressing regret for their inability to attend the presentation: Dr. Thomas B. Osborne, of New Haven, Conn.; Prof. Marston T. Bogert, of Columbia University, New York City; Prof. Charles Baskerville, of the College of the City of New York; Prof. W. A. Noyes, of the University of Illinois, and Prof. Rodney H. True, of the University of Pennsylvania. After reading the letters he stated that the meeting was open.

Dr. Charles D. Walcott, Secretary of the Smithsonian Institution, and President of the National Academy of Sciences, then read the following presentation address:

"Ladies and Gentlemen—We have gathered here this afternoon to do honor to Dr. Frederick Belding Power, who for fifty years has spent his thinking hours among the complicated molecules of organic compounds; who, because he possesses that peculiar faculty of exhausting each subject which he takes up, has had the greatest influence both in America and Great Britain in raising the standard of our pharmacopœias; who has gained distinction by his most difficult and life-consuming researches into the chemical composition of plant compounds.

"As a lasting tribute to these fifty years of research and in commemoration of those which he spent as director of the Wellcome Chemical Research Laboratories of London, I have been asked by Mr. Henry S. Wellcome, their founder, to present him with this gold medal, which bears the following inscription:

"To

FREDERICK B. POWER, PH. D., LL. D.

In recognition of his distinguished services to science  
during 18½ years as Director of the Wellcome Chemical  
Research Laboratories, London.

*Presented by the Founder,*

HENRY S. WELLCOME, 1914.

"Doctor Power graduated from the Philadelphia College of Pharmacy in 1874, in the same class with his life-long friend, Mr. Wellcome, who urged him to pursue his studies in Germany. He spent the years from 1876 to 1880 in Strassburg, becoming the assistant to Dr. Flückiger, one of the greatest pharmacologists of Europe. Returning to America, he spent nine years in the organizing and building up of the Department and School of Pharmacy in the University of Wisconsin, four years in researches on essential oils in a newly organized chemical works near New York, and in 1896 Mr. Wellcome appointed him Director of his chemical research laboratories in London. For eighteen and one-half years he devoted his time exclusively to chemical research and the direction of a staff of research workers under him. One hundred and fifty important scientific memoirs were published from the laboratories during this period. These covered a wide field of investigation for which material was obtained from all parts of the world. Among these a very notable and complete study was made of the East Indian chaulmoogra oil, which resulted in the discovery of some physiologically active acids of an entirely new type. These form the basis of the new treatment of leprosy, which gives promise of effecting a complete cure of one of the most terrible diseases of mankind.

"During these years in London Dr. Power had the opportunity of meeting and forming the close friendship of the foremost scientific men of Great Britain. The recognition of his work by the leading chemists and other scientists of Europe would be perhaps exemplified in the high tribute paid to him by the late Lord Moulton, one of the most learned and versatile men in Europe who was entrusted by Kitchener with the task of producing the high explosives for the war. Shortly before his death, he chided Mr. Wellcome for permitting Dr. Power (who for family reasons had returned to America) to leave Great Britain, for, as he remarked, 'there was no one in Europe who could fill his place.'

"In 1908 the University of Wisconsin, commemorating the twenty-fifth anniversary of the formation of its Department of Pharmacy, conferred upon Dr. Power, its founder, the degree of LL. D., and in 1913 the Chemical, Linnean and Pharmaceutical Societies of London awarded him the Hanbury gold medal, a distinction only once perviously bestowed upon an American. This was followed by the presentation of an illuminated address and an album containing the signatures of contributors from many parts of the world.

"Dr. Power, in recognition of your distinguished services to science, and in commemoration of the years which you spent as director of a laboratory devoted to chemical research, I have the honor to present to you this gold medal of appreciation from your life-long friend, Mr. Henry S. Wellcome, who, although with us this afternoon, is unfortunately prevented by a severe throat affection from

addressing us himself. He wishes to explain in presenting it that war conditions have prevented its earlier execution and presentation."

Dr. Power acknowledged the medal as follows:

"Dr. Walcott, I feel it to be a great honor to receive at your hands the beautiful medal which my friend, Mr. Wellcome, has so kindly and generously bestowed upon me, and I deeply appreciate the sentiments you have so eloquently expressed concerning my work. I can assure you Dr. Walcott and Mr. Wellcome, that this memento will always be regarded by me as one of my most precious possessions. It is difficult and well-nigh impossible on an occasion such as this to adequately express in spoken words the thoughts that are uppermost in my mind, for there are many happy recollections when a friendship formed in boyhood has continued uninterruptedly during a period nearly half a century. I cannot but be reminded that it is just twenty-five years ago this month when I left America for London to undertake the organization of the Chemical Research Laboratories which Mr. Wellcome desired to establish, and that the first public announcement of his purpose was made on the evening of July 21, 1896, in a beautiful salon of the great metropolis, where, by the invitation of Mr. Wellcome, a number of the most distinguished scientific men of England were assembled, whom it was my privilege to meet. One of the guests on that occasion was the late lamented Lord Moulton, whose brilliant legal career and service to science, especially during the strenuous years of the war, have won for him an enduring fame. The work that was so auspiciously inaugurated on that July evening it was my privilege to conduct for a period of eighteen and one-half years, and, although years of hard and earnest toil, they were replete with many happy associations, and I trust not without some benefit to the science that it was my endeavor to serve.

"There is one dominating thought that I should like particularly to convey to my friend, Mr. Wellcome, and that is embodied in an expression of gratitude. I am grateful for the encouragement and inspiration received from him on our journey through life, for we have traveled long and far together, but above and beyond all I am grateful for having possessed through so many years so kind, generous and true a friend. For this latest expression of your kindness, Mr. Wellcome, I beg you to accept my warmest thanks, and I desire also to extend my hearty thanks to Dr. Walcott for having so happily conveyed to me your beautiful gift."

Dr. Walcott then adjourned the formal meeting after inviting all those present to meet Dr. Power and to add a word of personal

appreciation to those given formally. A social hour followed, with light refreshments.

There was a distinguished gathering of notable persons present. Among the guests were:

Dr. Alexander Graham Bell; Hon. Robert Lansing; Dr. F. W. Clarke and Dr. David White, of the Geological Survey; Dr. Harvey W. Wiley; Dr. Carl L. Alsberg, Chief of the Bureau of Chemistry; Dr. W. A. Taylor, Chief of the Bureau of Plant Industry; Dr. L. O. Howard, Chief of the Bureau of Entomology; Dr. F. W. Coville, Dr. W. E. Safford, Prof. L. C. Corbett and Dr. O. Schreiner, of the Bureau of Plant Industry; Dr. Charles L. Parsons, Secretary of the American Chemical Society; Dr. W. F. Hillebrand, U. S. Bureau of Standards; Dr. Marcus Benjamin and Dr. J. N. Rose, of the Smithsonian Institution; Prof. Charles E. Munroe, National Research Council; Admiral Brownson, General R. E. Noble, of the Surgeon General's Office of the U. S. Army; Rear Admiral William C. Braisted, President of the Philadelphia College of Pharmacy and Science; Mr. Howard B. French, former President of the Philadelphia College of Pharmacy and Science; Hon. John B. Payne, former Secretary of the Interior; Rev. Charles Wood, Church of the Covenant; Senator Richardson; Dr. Atherton Seidell, of the Hygienic Laboratory; Mrs. (General) Gorgas; Professors Charles H. LaWall, E. Fullerton Cook and Julius W. Sturmer, and former President Otto W. Osterlund, of the Philadelphia College of Pharmacy and Science; Dr. Lyman F. Kebler, V. K. Chestnut, E. K. Nelson, and many others from the Bureau of Chemistry.

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#### THE MULFORD BIOLOGICAL EXPLORATION.

The early plans for the scientific expedition, known as the Mulford Biological Exploration of the Amazon Basin, were made public in an article appearing in the *AMERICAN JOURNAL OF PHARMACY*, issue of November, 1920.

The many groups of scientists and laymen who have shown such great interest in the plans for this work will be interested to know that the work is now under way, and that the expedition made its departure from New York on June 1st, under the most favorable circumstances.

The delay in getting the expedition into the field has been caused

by a chain of circumstances which have necessitated considerable changes in the original plan and in the route to be followed. One of the causes for the delay, which has given a great deal of concern to those interested, was the illness of the Director, Dr. H. H. Rusby, Dean of the College of Pharmacy of Columbia University. Dr. Rusby has been suffering from a severe and prolonged attack of pleuropneumonia, which struck him down very suddenly in the midst of active preparations for his trip. His many friends in the medical and pharmaceutical professions and among botanists will be pleased to learn that he is now well on the road to complete recovery.

The enforced delay has not been without benefit. From one point of view it has been of actual advantage, in that ample time was afforded for the elaboration of plans and preparations in the greatest possible detail. It has also resulted in the enlargement of the scope of the work to be undertaken and in the personnel of the party.

Membership in the party as now constituted, includes Dr. H. H. Rusby, as Director, who will be accompanied by a secretary, personal assistant and taxidermist in the person of George S. McCarty, a young man of sportsman-like qualities and training, from a well-known family of Woodbury, N. J.

Dr. Rusby will also be accompanied by Dr. Wm. M. Mann, an Entomologist of the Bureau of Entomology, U. S. Department of Agriculture, and Honorary Custodian in the Division of Insects, U. S. National Museum. Dr. Mann is an explorer and collector of wide experience in tropical travel.

E. N. Pearson joins the party as Ichthyologist, representing Dr. C. H. Eigenmann, of the University of Indiana, and Dr. A. G. Ruthven, of the University of Minnesota.

The botanical work of the expedition will be greatly increased by the addition to the party of Dr. Orland E. White, of the Brooklyn Botanic Garden, who goes as representative of the Brooklyn Botanic Garden and of the Bussey Institution of Harvard University.

He will devote his energies to the collection of orchids for Dr. Ames, and to the study of the economic botany of the regions covered.

The complete study of the medicinal products will occupy the attention of many specialists. Dr. Rusby will himself undertake

their botanical classification and description. Their microscopical study will be pursued by Dr. Ballard at the Columbia University School of Pharmacy by Professor Youngken, Philadelphia College of Pharmacy and Science, Schneider of Nebraska, Newcomb of Minnesota, and others. Their chemistry will be studied by Army of Columbia, Jordan of Purdue, Sayre and Havenhill of Kansas. The study of their physiological and medicinal properties will occupy the attention of many medical men at Yale, Harvard, the University of Pennsylvania, Johns Hopkins, and connected with the American Medical Association headquarters at Chicago.

Among other subjects of interest, is that of oil-seeds, of which there is a vast variety in the forests of tropical America. From fifty to a hundred pounds or more of each of these will be collected as encountered and these will be shipped home for expression and the study of their oils. Professor Augustus A. Gill, of the Boston Institute of Technology has undertaken to pursue these researches. Similarly there are very many plants containing essential oils that are likely to prove of value, and Dr. Edward Kremers, of the University of Wisconsin will interest himself in the study of these. The region to be traversed abounds in serpents and other reptiles, both poisonous and innocent. These will be preserved like the fishes. The batrachians will be sent to Professor Ruthven, of the University of Michigan, and the others to the American Museum of Natural History in New York City.

Special interest attaches to the arrangements recently completed, by which Dr. F. L. Hoffman, Vice-President and Chief Statistician of the Prudential Life Insurance Company, will accompany Dr. Rusby and his party for at least part of the journey. Dr. Hoffman, as one of the Directors of the American Public Health Association, and one of the leaders in the public health movement, has been interested in the plans for this expedition from the beginning. He joins the expedition with a very broad object in view, being especially interested in the health, longevity and sanitary progress in the regions visited, particularly as regards American residents, temporarily or permanently settled under conditions of tropical life. Knowing the rich natural resources of these regions he shares with Dr. Rusby a vision of the possibilities of wonderful development along many lines—a development which is now greatly retarded chiefly on account of an unfavorable environment and a high mortality, due

largely to diseases caused by insects and parasites of various kinds, which sap the vitality of the people.

Dr. Hoffman's efforts will be directed toward the accumulation and correlation of as much information as possible on these subjects. In fact it is planned to stress the economic phases of the entire work of the expedition with the aim of adding much to the knowledge necessary before any practical means can be employed to lessen mortality; to improve the environment and to make life more comfortable and worth living under tropical conditions.

From the library of the Prudential Insurance Company at Newark, the expedition has been supplied with copies of the latest maps of the regions to be visited, and copies of important publications and records of previous expeditions and notes on the tropical diseases occurring there—all of which will contribute greatly to the success of the work.

The change in the date of departure has made necessary a complete reversal of itinerary, in order to take advantage of the dry season north and south of the equator. Dr. Rusby and party will proceed directly to La Paz, Bolivia, from which city they will set out about July 1st, their first objective being the town of Rurenabaque, on the eastern side of the Andes. Here temporary headquarters will be established while the surrounding regions are being explored. Some of the party will proceed thither via the La Paz River, making collections en route in previously untouched territory. Others of the party, with the main portion of the cargo, will go by way of the Guggenheim Mines of the Bopi River. The first part of this journey is over a fine automobile road built by the Guggenheim Brothers to their large mines near Asunto. Both Mr. Daniel and Mr. Murray Guggenheim are active and generous officers and managers of the New York Botanical Gardens, and are largely interested in this expedition. They have promised every assistance that their representatives in Bolivia can render.

The next objective will be Lake Rocagua, in which region they expect to spend a month or more exploring and collecting. Other important collections will be made in the Valleys of the Rio Beni and the Mamore. The Mamore River will be visited with the special object of exploring the region which yields Brazilian Ipecac. Temporary headquarters will next be established at Villa Bella, the western terminus of the Madeira-Mamore Railroad. The party will so

arrange their work and time their journey as to reach Manaos about November of this year. Here they will receive large shipments of supplies for the second half of the journey and send home the collections already made.

According to present plans the party will then start out from Manaos early in 1922, ascending the Rio Negro and Rio Uaupes for the purpose of exploring and collecting among the upper waters of the latter river and in some of the valleys and ravines along the eastern side of the Andes, south of Bogota, Colombia. After crossing the mountains to Bogota, they will finally emerge at the coast at Baranquilla for their return journey.

To many experienced tropical travelers the plans for the second half of this journey from Manaos to Bogota appear to be somewhat venturesome and impractical because the party may be expected to be very much exhausted upon their arrival at Manaos. Dr. Rusby is confident, however, they will all arrive at Manaos in good health and, after a short rest, will be in good condition to undertake the second half of their journey.

Perhaps no other expedition that has gone into South America has ever entered the tropics so well protected medically against possibilities of fevers, skin diseases and the numerous tropical affections. The medical supplies which the expedition is taking includes a very long list of standard pharmaceuticals and a number of biological products, which are of even greater importance under the circumstances. These include great quantities of antidysenteric serum, for the prompt treatment of cases of dysentery, should any of the members of the party contract that disease,—a rather unlikely event if all the members make the proper use of the means provided for the sterilization of the drinking water. Antipneumococcic Serum and antitetanus serum are also included among the supplies. Most important, however, is a quantity of anti-snake-venom, which the Mulford Company took special pains to prepare for Dr. Rusby's party and which they are supplying to them in small, sterile, hypodermic syringes, ready for instant use when occasion requires.

Members of the party have further protected themselves against disease by taking certain preventive measures. These include the well-known measures of vaccination against smallpox and the prophylactic inoculations against Typhoid Fever, the effectiveness of which no longer remains a matter of doubt. In view of the



prevalence and dangers of pneumonia, to which they are exposed, especially in the highlands of Bolivia, the members of the party have been provided with an antipneumonia vaccine, which should give them considerable protection, for some time at least. If it gives them a moderate protection against pneumonia for even six or eight weeks, this will carry them over the most dangerous period, *i. e.*, until they have crossed the Andes and have descended from the highlands of Bolivia to the great plains. They are also supplied with various insecticides and repellents which they will use to obtain relief from the annoyance of incessant attacks of hordes of insects.

Through Dr. Rusby's wide experience and foresight, all the possible needs of the party while in the field have been provided for in great detail. Among the supplies are large quantities of food-stuffs, such as canned meats, bacon, etc., purchased from surplus Army stores, and also a quantity of evaporated vegetables and soup powders. Their supplies and equipment, weighing nearly three tons, is packed in a large number of boxes of the proper size for transportation by mule or human porters.

The scientific work of the expedition is well provided for in the form of all kinds of scientific apparatus, collecting equipment and containers with abundant supplies of formaldehyde and other preservatives. A full supply of printed labels and note-books are among the details provided, so that collections may be sent back properly identified and ready for study.

The active support and co-operation which has come to Dr. Rusby from so many quarters is a source of much gratification, and the many offers of assistance and tokens of interest and esteem have greatly encouraged the members of the party as they start out on this most difficult undertaking.

The officials of the H. K. Mulford Company, which house is acting as sponsor and financial backer of this enterprise, have been especially gratified at the generous attitude which institutions of learning and Government Bureaus have taken toward this expedition.

The hope has been expressed in many quarters that the successful outcome of this enterprise will convince scientists and the public generally that complete and hearty co-operation between large industrial and scientific institutions can be obtained to their mutual benefit and on a thoroughly professional and altruistic basis.

## ABSTRACTED AND REPRINTED ARTICLES

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### A COLOR REACTION FOR ACONITE.\*

By S. MALLANNEH, M. D., D. P. H.

The color reactions at present known are not reactions of aconitine, but of benzoic acid, which is one of the products of decomposition of aconitine. Hence the color reactions are not specific.

Most of the color reactions for alkaloids are such that they are useful only when applied to pure samples of alkaloids, but they are of no use when applied to crude substances containing alkaloids.

In medico-legal cases, especially in India, the poisoning is generally caused by the administration of crude substances in the form of powdered root, bark, or seeds, and not by the use of active principles. If the quantity of the vegetable poison present in the stomach be small, as is generally the case with aconite, it is next to impossible in most cases to get a sufficient amount of alkaloid extracted in order to prove the presence of poison by means of experiments on animals.

In India the vegetable poison also undergoes decomposition so quickly that it is almost impossible to detect its presence in a dead body, though distinct clinical symptoms of poisoning might have been present before death. But the cause of the failure to detect the poison in such cases is that, up to date, there is no reliable chemical test known for aconite.

As the result of my experiments, I have discovered a test which I think is very useful for medico-legal purposes. If a minute particle of potassium ferricyanide be placed close to a minute portion of aconitine or a small portion of powdered root of aconite, and then a drop of formic acid added, a green coloration immediately appears. This is every delicate reaction as 1/8000 grain of aconitine gives a positive reaction. Heat should not be applied for this test.

Morphine, atropine, digitalin, strychnine, eserine and hyoscy-

\* Reprinted from *The Analyst*, May, 1921.

mine do not react to this test, which therefore seems to be specific for aconite. It is not only applicable to the pure alkaloid, but also applicable to powdered root of aconite. Hence, if confirmed, it will be of great toxicological importance. Recently, in a case of human poisoning at Banswada Nizamaabad, I was able to test this reaction. A few black fragments found adherent to the stomach wall of the deceased gave positive reaction to this test, and the case was confirmed subsequently by experiments on animals. The police were able to procure from the house of the culprit a brown powder, which on examination was found to be powdered root of aconite.

#### DISCUSSION.

Mr. H. Finnemore said that, apart from the limited value of all color reactions, this test was not specific for aconitine, since it appeared to be given by the Indian variety of aconite, which contained pseudoaconitine, but not aconitine.

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### WOOD DISTILLATION.

#### *Census Bureau's Summary Concerning the Industry, 1919.*

A preliminary statement of the general results of the 1919 census of manufactures with reference to the wood distillation industry has been issued by William M. Steuart, Director, Bureau of the Census, Department of Commerce. It consists of a detailed statement of the quantities and values of the various products manufactured, prepared under the direction of Mr. Eugene F. Hartley, Chief Statistician for Manufactures.

Reports were received from 116 establishments engaged in the distillation of wood, and their products for the year were valued at \$32,635,000. At the census of 1914 there were 101 establishments, with products valued at \$10,530,000. The value of annual production has therefore increased \$22,105,000, or 209.9 per cent.

In 1919, 44 establishments were located in Pennsylvania, 21 in New York, 16 in Michigan, 7 in Georgia, 6 in Florida, 4 in Alabama, 4 in Louisiana, 3 in Wisconsin, 2 in Mississippi, 2 in North Carolina, and 1 each in Connecticut, Kentucky, Missouri, New Jersey, Tennessee, Texas and West Virginia.

The statistics for 1919 and 1914 are summarized in the follow-

ing statement. These figures are preliminary and subject to such change and correction as may be necessary from a further examination of the original reports.

*Comparative Summary of Statistics for the Wood Distillation Industry, 1919 and 1914.*

	1919.	1914.
Number of establishments <sup>1</sup> .....	116	101
Value of products <sup>1</sup> .....	\$32,635,000	\$10,530,000
<hr/>		
Wood alcohol (for sale):		
Crude .....	Gals. 6,981,000	7,197,000
Value	\$5,593,500	\$1,605,900
Refined .....	Gals. 6,985,000	6,235,000
Value	\$8,381,900	\$2,709,400
Acetate of lime .....	Lbs. 152,064,000	163,522,000
Value	\$2,682,200	\$2,138,900
Turpentine, wood .....	Gals. 1,521,000	575,600
Value	\$1,207,700	\$194,200
Rosin, wood .....	Bbls. (280 Lbs.) <sup>2</sup> 234,000	51,800
Value	\$2,742,600	\$198,200
Charcoal .....	Bush. 48,499,000	44,828,000
Value	\$8,231,400	\$2,829,600
Other wood products and derivatives....	<sup>3</sup> \$3,243,000	\$626,300
All other products .....	\$552,700	\$227,500
<hr/>		
<i>Materials.</i>		
Wood .....	Cost \$8,323,000	.....
Hard woods .....	Cords 1,019,500	970,300
Pine .....	Cords 255,700	72,200
Crude wood alcohol purchased .....	Gals. 7,300,000	5,665,000
Cost	\$5,898,000	\$1,408,000

<sup>1</sup> Includes one establishment in 1919, and six in 1914, engaged primarily in other industries; subsidiary products in 1914, \$647,292.

<sup>2</sup> Includes 12,254 bbls. reclaimed from gum rosin dross.

<sup>3</sup> Includes for 1919: Tar oil, 803,440 gals., \$240,805; tar, 2,143,157 gals., \$481,820; wood creosote, 1,152,655 lbs., \$31,957; methyl acetone, 930,253 lbs., \$134,166; ketone, 209,084 lbs., \$52,141, and formaldehyde, acetone and acetone oil, each the product of two establishments, and acetic acid and acetate of soda, each one establishment.

## SCIENTIFIC AND TECHNICAL ABSTRACTS

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TOXICITY OF THYMOL AND CARVACROL.—Dr. A. E. Livingston, of the Hygienic Laboratory, has recently published the results of an extensive investigation of the comparative toxicity of thymol and carvacrol. He reports: the toxicity of thymol and carvacrol on rabbits is essentially the same; the toxicity of thymol and carvacrol as tested on paramecia shows no striking difference; tests on earthworms indicate that the relative anthelmintic values of thymol and carvacrol are practically the same. (*J. Pharm. Exp. Ther.*, Vol. 17, p, 261, 1921.)

J. F. C.

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IDENTIFICATION OF TR. COLCHICUM.—Glücksman suggests the following procedure for the identifying of this tincture: 1. A dull yellow solution results from the mixing of 1 ml. Tr. Colchicum and 9 ml. conc. hydrochloric acid. 2. Mayer's test. 3. 25 ml. of tincture to which is added 0.5 Gm. paraffin are evaporated with shaking on the steam bath shaken up with 6 ml. of distilled water, cooled, filtered, the residue washed and the filtrate evaporated to dryness, extractor with 10 ml. warm chloroform and filtered after adding a little asbestos. The chloroform is evaporated off, the residue is dissolved in about 5 ml. of water and filtered if necessary. The clear solution is treated with 1 to 2 drops of 10 per cent. ferric chloride solution and 10 drops of strong hydrochloric acid, and is maintained several minutes at the boiling point in order to convert the colchicine into colchicein. By this treatment the green color which develops becomes more intense. If this is not sufficiently decisive the cooled solution is shaken with an equal volume of chloroform, which, after several days, becomes colored cherry red. (*Apoth.-Ztg. der tschechoslowakischen Republic*, 1920, p. 328.)

J. F. C.

CUPRESSUS SEMPERVIRENS IN THE TREATMENT OF HEMORRHOIDS.—The cypress has vaso-constrictive properties analogous to hamamelis; these are even more marked and more constant than those of the latter. The fluidextract, tincture or soft extract may be given internally in doses which represent from 10 to 30 grains twice a day. For local application the tincture or fluidextract may be made into a lotion, the soft extract may be used in an ointment or in suppositories. Good results have followed this treatment. (Leclerc, *Bull. Soc. Thérap.*, 1920, p. 184.)

J. F. C.

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COTTON'S PROCESS ETHER.—Some time ago, J. H. Cotton<sup>1</sup> claimed that there were present in anæsthetic ethers two classes of extraneous substances: one class including substances favorable to the production and maintenance of anæsthesia and which were really synergists, while the other class consisted of undesirable impurities, which cause post-operative nausea, irritation of the respiratory tract, and other symptoms generally recognized as "ether sickness." He said that by supercharging purified ether with the beneficial synergists—ethylene and carbon dioxide—he could produce a condition of analgesia, without loss of consciousness, with less ether than was necessary for surgical anæsthesia.

This new ether has been reported on by J. E. Lumbard,<sup>2</sup> who found that pure ether, 99.8 per cent., simply acted like a very weak ether, while ordinary 96 per cent. ether produced satisfactory anæsthesia on the same patients. The ideal ether, he thinks, would therefore be a superior grade of ether from which toxic properties had been eliminated, afterwards recharged with the synergists in suitable proportion, just as Cotton claims. Such an ether he has tried in over 400 cases, and he concludes that it certainly acts like a stronger ether, at least during the stage of induction, in which there is apparently less irritation of the mucous membranes and less secretion of mucus. During the stage of maintenance little difference was noted, unless possibly that a smaller amount of ether was used. Recovery seemed less disturbed than when using ordinary ethers, and post-anæsthetic effects were minimized. There is greater tendency

<sup>1</sup> *Amer. J. Surg.*, April, 1919, p. 34.

<sup>2</sup> *Ibid.*, October, 1920.

to cyanosis, and patients have to be more carefully watched. Analgesia by Cotton's ether is apparently identical with primary anæsthesia such as can be obtained with any other anæsthetic, but it is possible with the new ether to maintain the analgesic state for a much longer time, with the patient fully conscious and with fairly good control of all voluntary muscles. (From the *Prescriber*, No. 176, 194; May, 1921.)

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PREPARATION OF PURE CARBON DIOXIDE.—Robert Crosbie Farmer, of the Royal Arsenal, Woolwich, prepares carbon dioxide completely free from air by the reaction between potassium hydrogen carbonate and sulphuric acid. Carbon dioxide is passed through a solution of potassium hydrogen carbonate (300 grams to the litre) and also through a solution of sulphuric acid (120 cc. diluted to 1 litre); the solutions are thus rendered free from dissolved air; they are then caused to react in an air-free vessel; and pure carbon dioxide, entirely free from air, is obtained. The product is so pure that it gives practically no gaseous residue on absorption with potassium hydroxide solution. (*Journal of the Chemical Society*, 1920, cxvii, 1446-1447; through *Journ. of the Franklin Inst.*, Feb., 1921.)

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A QUALITATIVE REACTION FOR MAGNESIUM.—F. Eisenlohr describes the following test for magnesium. An alcoholic solution of alkanet root is prepared and to 5 cc. of it is added a drop of ammonium carbonate solution of 2N strength. This produces no appreciable change of color, but if additions are made of a few drops of neutral solutions of either magnesium, barium, calcium, strontium or manganous salts the following effects are respectively produced:

Magnesium	Barium	Calcium	Strontium	Manganese (ous)
blue violet	no change	blue	blue violet	blue violet

The colorations produced by magnesium, strontium and manganous salts are not strikingly different, but if the solution is acidified with not more than two drops of 2N hydrochloric acid, the liquid changes to bright red, and then, if again rendered alkaline by a like volume of ammonium carbonate solution, becomes, in the presence of magnesium, blue violet. In dealing with an ordinary phosphate precipitate, this is dissolved in 2N hydrochloric acid, and a

portion of the alkanet solution is mixed with a drop of the acid solution, and then one to two drops of the ammonium carbonate solution, when the presence of a magnesium compound will be shown by the production of the blue violet. If magnesium is not present, the original color of the alkanet solution will appear.

The alkanet solution must not be diluted with water, as this will give rise to a hydrolysis of the ammonium carbonate by which ammonium hydroxide will be produced (*Ber.*, 1920, Vol. liii, 176; through *Journ. Franklin Inst.*, Feb., 1921.)

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## MEDICAL AND PHARMACEUTICAL NOTES

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ANTIBODY STUDIES.—*The Journal of Immunology*, for March, 1921, was devoted exclusively to the publication of "Antibody Studies," by Dr. F. M. Huntoon, of the Mulford Biological Laboratories, Glenolden, Pa.

These papers cover a vast amount of original research work, on a very important subject, and have to do with extracting the protective substances or antibodies from bacterial serums, such as Antipneumococcic Serum, Antimeningococcic Serum, etc.

The results of Dr. Huntoon's work hold promise of a new epoch in the serum treatment of pneumonia, and possibly some of the other infectious diseases. Dr. Huntoon was able to produce sterile extracts of the pneumococcic protective antibody, possessing approximately the same antibody content as the best immune serum, and yet very low in serum protein content.

We are informed that these extracts have not yet been placed on the market, but their clinical value is being carefully determined in a number of leading hospitals, and we are assured that if the results continue satisfactory, these antibody extracts will be made available by the Mulford Laboratories as soon as possible, for the benefit of the medical profession, and humanity at large.

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LOBINOL—THE POISON OF POISON OAK.—James B. McNair has extracted a dermatitant, or poison, producing inflammation of the skin, from the poison oak *Rhus diversiloba*. The bark was extracted



with alcohol; and the extracted poison was purified by successive treatments with petroleum, ether, alcohol, sodium chloride brine, and distilled water. The poison apparently is an unsaturated compound of the aromatic series, containing carbon, hydrogen, and oxygen; it reacts like a phenol, and may contain two hydroxyl groups in the ortho position. On account of its phenolic nature, it has been named lobinol. (*Journ. Amer. Chem. Soc.*, 1921, xliii, 159-164; through *Journ. Frank. Inst.*, Feb., 1921.)

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## NEWS ITEMS AND PERSONAL NOTES

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FUNDS FOR SCIENTIFIC RESEARCH.—The Research Information Service of the National Research Council has recently compiled information about funds for scientific research. From this compilation it appears that there are hundreds of special funds, trusts, or foundations for the encouragement or support of a research, in the mathematical, physical and biological sciences, and their applications in engineering, medicine, agriculture and other useful arts. The income from these funds, which amounts annually to at least fifty million dollars, is used principally for prizes, medals, research scholarships and fellowships, grants and sustains appropriations or endowments.

So numerous have been the requests to the Research Council for information about sources of research funds, availability of support for specific projects and mode of administration of particular trusts or foundations, that the Research Information Service has created a special file, which it is proposed to keep up to date in order to answer the questions of those interested in such funds. Furthermore, in order to give wider publicity to the immediately available information about research funds, the Council has issued a bulletin under the title "*Funds Available in 1920 in the United States of America for the Encouragement of Scientific Research.*"

Inquiries concerning the bulletin or for information about research funds should be addressed, National Research Council, Information Service, 1701 Massachusetts Avenue, Washington, D. C.

INFORMATION BUREAU OF THE NATIONAL RESEARCH COUNCIL.  
—Many scientists lack the library facilities which their work demands. They are compelled either to journey to distant libraries or to try to borrow books by mail. Often it is difficult for them to locate some thing that is badly needed, and again it may be impossible to borrow it.

The Research Information Service of the National Research Council is prepared to assist investigators by locating scientific publications which are not generally or readily accessible. It will also, as is desired, have manuscripts, printed matter or illustrations copied by photostat or typewriter. The cost of copying varies from ten to twenty-five cents per page. No charge is made for this service unless an advance estimate of cost has been submitted and approved by correspondent.

Requests for assistance should be addressed, National Research Council, Information Service, 1701 Massachusetts Avenue, Washington, D. C.

# THE AMERICAN JOURNAL OF PHARMACY

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## EDITORIAL

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### A BOUNDEN DUTY.

In the July, 1920, issue of this JOURNAL is an editorial, written by Mr. George M. Beringer, and entitled "The End of the Law is Obedience." Cleverly and carefully written, and chiefly concerned with a criticism of the attitude of certain pharmaceutical organizations in regard to the enforcement of Prohibition, it merits at this date, one year after its writing, a thorough study and an understanding of its deft argumentations.

Let the reader consult his files of the JOURNAL, turn to this editorial and read it once again. It is as pertinently impertinent and as impertinently pertinent today as upon the day of its writing.

We were drawn to it after looking over a certain resolution drafted and endorsed by the Pennsylvania Pharmaceutical Association, upon recommendation of the President, Mr. Sturgeon, at their recent meeting in Philadelphia. The particular resolution referred to follows:

*"Whereas*, the authorities at Washington have, without consulting the leaders of the drug industry and decidedly contrary to their wishes attempted to force the burden of carrying out the provisions of the Volstead Act upon the shoulders of the retail druggists, thus arbitrarily shifting the outlawed business of the saloon upon the druggists of the country, and

*"Whereas*, such action upon the part of the Treasury Department and the Internal Revenue Commissioner is repugnant to the reputable members of our profession and is hereby resented, therefore be it

*"Resolved*, that we earnestly recommend that no member of the Pennsylvania Pharmaceutical Association will permit himself or his pharmacy to be degraded in the estimation of the public by falling into the trap that has been laid to bring our business into disrepute by dispensing beer and wine, even upon physician's prescription, even under the false guise of their being for medicinal purposes."

The resolution does not bear a keen dissection, and, except for a high-sounding note of pseudo-altruism, there is nothing in it that savors of worthiness. That the Pennsylvania Pharmaceutical Association adopted such a creed is no unusual compliment to that usually carefully conducted body, except as we may look upon its adoption as having been hasty and without deliberation. The editorial referred to adeptly sums up our criticism of this poorly constructed resolution in the following statements:

"It is inconceivable that anywhere in these United States, it should not be recognized that the Eighteenth Amendment *prohibited* the manufacture, sale, transportation, importation or exportation of intoxicating liquors; that this and the Enforcement Act have outlawed 'the business of the saloon.' It is incomprehensible that a deliberate body, such as a pharmaceutical association is supposed to be, would now resolute about a business that the will of the people and the laws of the land had outlawed and even more so that they would even suggest that such a disreputable business was to be by the 'Government' 'forced' upon the retail druggist.

"The Volstead Act recognizes that the use of alcoholic liquors is necessary for the extraction, solution and preservation of medicinal preparation and rightly provides the means by which the druggist may obtain the supplies required for such uses. Further, that at times, certain distilled spirits and wines are considered by the attending physician as a therapeutic necessity, and it very carefully prescribes methods by which the physician may issue prescriptions for these in limited quantities, and then very rightly *considering that they are medicines directs that these shall be filled only through a pharmacist 'duly licensed under the laws of his State to compound and dispense medicine prescribed by a duly licensed physician.'* Is it not the legitimate duty of the licensed pharmacist and of no one else to dispense medicines? Is not this the very basic principle that has justified the enactment of pharmacy laws for the protection of the public against promiscuous and incompetent dispensing?

"This is an irrefutable statement of the law and the facts, and no perversion will justify an assertion or even an intimation that 'the Government' is desirous of providing for a continuation of 'the outlawed business of the saloon,' or of 'forcing it upon the retail druggist.'

"After all, the Mosaic injunction is a safe and worthy advice for pharmacists to follow:

"'According to the sentence of the law which they shall teach thee, and according to the judgment which they shall tell thee, thou shalt do; thou shalt not decline from the sentence which they shall shew thee, to the right hand, nor to the left.' (Deut. 17: 12.)"

In our opinion a far worthier resolution was the one offered by Dean LaWall, of Philadelphia, and also adopted:

*"Resolved, that the members of the Pennsylvania Pharmaceutical Association emphatically affirm that alcohol is a necessary solvent and preservative in the making of many valuable medicinal preparations, but we disapprove the illegal dispensing by pharmacists of alcoholic liquors or liquids, suitable for beverage purposes, and unanimously recommend the expulsion of any member convicted of such practice."*

The Pennsylvania Pharmaceutical Association is to be congratulated upon its adoption of the latter resolution, but is amenable to criticism for its unwarranted adoption of the other resolution, which, in correctness, should never have been offered in session.

I. G.

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## ORIGINAL PAPERS

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### COMPARATIVE RESEARCHES ON THE METHODS PROPOSED FOR THE ESTIMATION OF GLYCYRRHIZIN IN LICORICE ROOT AND IN LICORICE EXTRACT.

By ARMIN LINZ.

*(Prize Research of the Hagen-Bucholz Foundation, 1913-1914.)*  
*(Archiv der Pharmazie, 1916, Vol. 254, 65-134, and 204-224.)*

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TRANSLATED BY DR. PERCY A. HOUSEMAN. APRIL, 1921.

*(Continued From Page 414.)*

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In controlling this method I obtained from 2.5 g. licorice 0.240, 0.249, 0.256, 0.257 g. of ammonium glycyrrhizinate, *i. e.*, 9.44-10.08 per cent.

The losses determined on 5 g. licorice amounted to 0.91-1.32 per cent. They are thus less than in the majority of similar determinations. The high value for ammonium glycyrrhizinate, as well as the slight losses show that the method is a practical one. The favorable result is to be ascribed to the use of ice water, and to the low temperature maintained throughout. The detailed procedure is not practicable since the awkward arrangement of freezing gives no better results than allowing to stand in ice.

## 10. Houseman (1912).

"Two g. licorice are dissolved in 10 cc. hot water in a centrifuge tube. After cooling, 20 cc. of 80 per cent. alcohol are added, and then gradually 50 cc. of 95 per cent. alcohol. The tube is centrifuged after standing two hours, the residue is stirred up twice with 80 per cent. alcohol, and again centrifuged. The liquid is poured off, and evaporated to dryness on the water bath in vacuum. The residue is transferred with 30 cc. water, to a small Erlenmeyer flask, and the glycyrrhizin, after cooling to 15°, is precipitated with 3 cc. dilute sulphuric acid (10 cc.  $\text{H}_2\text{SO}_4$  to 300 cc. water). After standing two hours, the contents of the beaker are cooled for a half an hour in ice, and the clear liquid poured through a small filter. The glycyrrhizic acid is washed four times by decantation with ice water, the precipitated acid remaining in the flask, as well as any which has been transferred to the filter, is dissolved in dilute alcohol. Two drops of 5 per cent. ammonia are added to neutralize traces of sulphuric acid, and the solution evaporated to constant weight in a tared dish."

Houseman has modeled his method, as he himself states, upon that of Parry.

[TRANSLATOR'S NOTE.—This is not true. Parry obtained the translator's (Houseman) method confidentially, and published it as his own without acknowledgment. (P. A. H.)]

The new feature introduced is the centrifuge. The method has been worked out exactly by the author and gives detailed directions. He does not confine himself alone to the determination of glycyrrhizin, but also gives methods for determining the matters insoluble in cold and in hot water, starch, gums, and finally, sugar before and after inversion. Gums, etc., are precipitated by a large volume of alcohol. According to my view, as already stated in discussing Parry's method, a greater concentration of alcohol would have the danger of precipitating glycyrrhizin compounds. In order that any glycyrrhizin which is precipitated or remains undissolved, shall be obtained in the determination, Houseman centrifuges the precipitate twice more with 80 per cent. alcohol. The amount of alcohol used is, unfortunately, not stated. It would presumably answer the purpose, to warm the mixture somewhat before centrifuging, in order

that everything soluble might certainly be extracted. The alcoholic extract is to be evaporated, in vacuum, to dryness. Why this evaporation is to be carried so far, I cannot understand, and Houseman himself does not further offer reasons for the instruction. It suffices completely, to carry the evaporation until the alcohol is driven off. That Houseman has, in evaporating to dryness, reckoned with the possibility of decomposition, is proved by his care in evaporating in vacuo. I carried this out by connecting a water pump to the arm of a distilling flask and carefully evaporating. The heating took place on the water bath at as low a temperature as possible. Great care is necessary here on account of possible boiling over. In my opinion, this whole experimental arrangement is superfluous, since one can do without the unnecessary evaporation to dryness. The precipitation of glycyrrhizic acid takes place with dilute sulphuric, of the same strength used by Parry and Evans. Houseman allows the precipitated acid to stand only two hours, on the ground that 12 to 24 hours standing is superfluous, and gives lower results. I have observed the contrary and can here only state, that sulphuric acid, after standing longer than two hours, still gives a brown precipitate which sticks to the bottom of the vessel, and which is soluble in ammonia. According to my observations which I have made on a large number of analyses, standing from 10 to 12 hours is recommended. Houseman also makes use of the difficult solubility of glycyrrhizic acid in ice water, but avoids the false experimental conditions of Evans' Sons. He precipitates at 10°, and then places the vessel on ice. The purification of the acid, sticking on the bottom of the vessel, takes place by decanting four times with ice water. Unfortunately, Houseman mentions no quantities. I have already often stated that a good purification by decantation cannot well be carried out. The glycyrrhizic acid is weighed in this determination. When Houseman states in conclusion that he weighs pure glycyrrhizin, he is grossly deceiving himself.

[TRANSLATOR'S NOTE.—Houseman makes no such statement, but, on the contrary, expressly states that he weighs crude glycyrrhizin. It is Linz who is grossly deceiving himself. (P. A. H.)]

The end product shows exactly the same color as all the other preparations obtained in a similar way. I obtained from 2 g. licorice 0.189, 0.193, 0.2 g. glycyrrhizic acid, *i. e.*, 9.45-10.0 per cent. I de-

terminated the loss on 4 g. licorice. It corresponded to 1.0-1.25 per cent. of the licorice. The matter insoluble in the alcohol-water mixture was 50 per cent. In examining the method and the results I obtained with it, I found there are no serious objections to be made to it, and that it gives practical results.

*11. Tschirch-Erikson (1910).*

"Ten g. licorice extract are dissolved in a 100 g. cold water, 100 cc. of 90 per cent. alcohol are added with stirring, and the mixture warmed on the water bath for half an hour. It is then filtered, and washed with 50 cc. hot alcohol. The alcohol is removed from the filtrate on the water bath, and the volume made up to 200 cc. with distilled water in a volumetric flask.

Glycyrrhizin: 40 cc. of this solution are taken out with a pipette, and 25 per cent. sulphuric acid is added as long as a precipitate forms. After standing two to three hours it is filtered through a small filter, and washed with 5 per cent. sulphuric. The filter with the residue is heated for a quarter of an hour on a water bath, in a small porcelain dish, with 50 cc. 90 per cent. alcohol. It is then filtered and 30 cc. water added. After driving off the alcohol, another 30 cc. of water and then 25 per cent. sulphuric acid are added until the glycyrrhizin is precipitated. After standing for one hour, the liquid is filtered through a small filter, and the latter treated with 5 per cent. cold alkali. After solution has occurred, it is filtered at once into a potash-glass flask, fitted with a reflux tube, and the filter is washed out with 100 cc. water. 120 cc. Fehling solution are then added and boiled for 15 hours. The precipitated  $\text{Cu}_2\text{O}$  is determined according to Allihn, and the glucose number found is calculated to glycyrrhizic acid according to the equation:

$$360 : 896 = \text{quantity of glucose} : X."$$

The method of Tschirch-Erikson is of great significance. It points out an entirely new way to a complete assay of licorice root and extract. In checking up this method I shall not adhere strictly to the title of my subject, but shall also examine Erikson's proposal for the determination of sugars. I believe this is all the more necessary, since as can be easily seen, the determination of sugars is difficult to separate from that of glycyrrhizin in this method for licorice



extract, and in the case of root, cannot be separated from it at all. If I take a long time over this work, this is done because at the time it was published, it was taken up in all the journals, including the foreign ones, and was praised by them. Further, a detailed control of the method does not appear to have been attempted by them. But above all, because the name of the author appears to guarantee that Tschirch's method could perhaps be accepted without such a control. The hydrolysis of glycyrrhizic acid appears to have been finally explained and established by formulas by Tschirch and his pupils.<sup>1</sup> By the hydrolysis with acids or alkalis, there is formed from glycyrrhizic acid, glycyrrhetic acid and glucuronic acid.

I here quote Erikson word for word, "As an aldehyde, glucuronic acid reduces Fehling solution, and if it is possible to decompose glycyrrhizic acid quantitatively into its components, a process based on this reduction must lead easily to a quantitative determination." "On the reducing capacity of the glucuronic acid, split off by hydrolysis, Tschirch has based his method for the determination of glycyrrhizin. And since both glucose and saccharose also reduce Fehling solution, but under different conditions, so must the three most important ingredients of licorice root (and Erikson also arrived at this conclusion), be capable of quantitative determination through their behavior towards this reagent."

The method stands or falls by the answer to the question: Can glycyrrhizic acid be determined quantitatively by hydrolysis by means of Fehling solution? Unfortunately I must definitely answer this question in the negative. Although the proof of this statement would prove the inadequacy of the method, I wish to enter into the whole procedure of the method, because it contains, both theoretically and practically, a good deal which is open to controversy.

[TRANSLATOR'S NOTE.—Linz then proceeds to the fact that an exact quantity of sulphuric acid is not specified, particularly in washing with 5 per cent. sulphuric acid. He found that heating the alcohol-sulphuric acid solution for a quarter of an hour carbonized the solution, and mentions a whole series of other manipulative difficulties. He thinks an actual oversight occurs at one place in Tschirch's method, and that Tschirch intends potash to be used, but omits to say

<sup>1</sup> *Archiv d. Pharm.*, 245, 97; 246, 545.

so. He further objects to Erikson precipitating the glycyrrhizin present in 2 g. licorice, from as much as 60 cc. of water, as this entails a serious loss through solubility. Linz claims that the question: Is glycyrrhizin quantitatively decomposed by hydrolysis? is as yet unsolved.

Linz then conclusively proves that Tschirch's method of hydrolysis with Fehling solution does not work.

After	4 hrs.	heating	Linz	obtained	0.0388	CuO = 0.054 g.	glycyrrhizin.
"	8	"	"	"	0.1078	CuO = 0.109 g.	"
"	12	"	"	"	0.2941	CuO = 0.302 g.	"
"	15	"	"	"	0.3041	CuO = 0.312 g.	"

When Linz makes a blank experiment, without any glycyrrhizin present, he obtains a large quantity of red cuprous oxide after two hours' boiling, which increases as the boiling is continued.

Linz therefore concludes "The decomposition of the alkali and copper tartrate, by strong heating, is very appreciable, and makes its use in the method given by Tschirch impossible. Thereby Tschirch's proposal to determine glycyrrhizin quantitatively by hydrolysis with Fehling solution falls to the ground."

Linz then shows that the self-reduction of Fehling solution has already been known in the literature, that it must be serious in 15 hours boiling, that the degree of alkalinity and the solution volume also affect the action of Fehling solution, and that there is a tendency to oxidation as well as reduction during 15 hours boiling. (P. A. H.)]

Linz concludes:

"I will summarize my objection to Tschirch's idea and to Erikson's procedure as follows:

"The proof that the hydrolysis of glycyrrhizin runs quantitatively is not attempted, and is not established.

"On the contrary, I have proved that a quantitative hydrolysis with Fehling solution cannot be carried out, because the copper or cuprous oxide weighed is derived in large part from self-reduction of the Fehling solution.

"Before the actual process of hydrolysis begins, appreciable quantities are lost, of the substance to be determined.

"The end point of the hydrolysis cannot be sharply established."

*The Tschirch-Erikson Sugar Determination.*

[TRANSLATOR'S NOTE.—Linz goes on to show that the determination of glucose, by allowing the filtrate from the glycyrrhizin to stand overnight in the cold with Fehling solution, is quite inaccurate, Erikson speaking of carrying out this method "according to Allihn," but not following Allihn at all as to method. Erikson does not attempt to prove the accuracy of this proposed new method, and she would have failed had she attempted it. The impossibility of the Tschirch-Erikson method is so evident, that the translator considers it unnecessary to enter into the full details of Linz's discussion. (P. A. H.)]

Linz summarizes as follows:

"The experimental method of Erikson cannot be used because it does not give correct results for the glucose content of licorice extract. Erikson has not attempted to test her glucose determination on pure grape sugar. Such a test would have convinced her of the inaccuracy of her method. She also takes no account of the peculiarity of Fehling solution to dissolve the separated cuprous oxide by oxidation."

[TRANSLATOR'S NOTE.—Linz goes on to prove that the method given for saccharose (filtrate from glucose determination, boiled three minutes with more Fehling solution) is also quite incorrect. He shows that saccharose needs preliminary inversion. Also that Erikson did not test the method on pure cane sugar, which, as expected, gave Linz a negative result.

It is unnecessary to enter into Linz experimental details which undoubtedly refute the Tschirch-Erikson method. (P. A. H.)]

Linz says "In summarizing this part of Tschirch's method, as carried out by Erikson, I cannot avoid accusing the latter of proposing a new method, without having beforehand, by suitable testing, convinced herself of its accuracy. . . . Not only the glycyrrhizin determination, but also that of the individual sugars cannot give accurate results. This is not due alone to the practical work of Erikson. Tschirch's method itself unfortunately cannot be used quantitatively."

*12. Guignard (1912).*

"Five g. licorice are dissolved to 500 cc. with water. To 125 cc. of this solution in a half liter beaker, there is added in a thin stream, 250 cc. 95 per cent. alcohol. After standing 24 hours, and filtering,

300 cc. of the filtrate, corresponding to 1 g. of the licorice extract, is evaporated to a syrup on the water bath. In a control experiment, it is determined whether in the solution of this extract in 5 g. of water, gum is precipitated by Telle's method. If this does not occur, the solution in 5 cc. of water is treated, after cooling, with 1 cc. sulphuric acid (diluted with the same quantity of water) and allowed to stand. It is then decanted, washed three times with 2 cc. portions of water, the residue dissolved in ammonia, evaporated, and weighed to constancy."

Guignard by his method saves the troublesome time-consuming filtration. Whether accurate results are obtainable by his method seems to me to be doubtful. Theoretically I consider this to be impossible. Guignard makes up to 500 cc., pipettes out 125 cc., then adds 250 cc. alcohol; 300 cc. are then to be measured exactly. This contains the alcohol-soluble material of 1 g. licorice. But this is only the case when one works really exactly and always uses pipettes. I call attention here to the contraction in volume of an alcohol-water mixture, as well as to loss of liquid by evaporation of the alcohol during 24 hours standing. Even careful covering can hardly prevent this evaporation.

[TRANSLATOR'S NOTE.—Linz considers that the test for gums according to Telle is superfluous. He also considers the conditions of washing by decantation unsatisfactory, and that ammonium sulphate will be present in the product weighed. He objects to the fact that less than a decigram of ammonium glycyrrhizinate is weighed. This results in large inaccuracies. Linz concludes "I cannot therefore agree with the author's conclusion 'the method proposed by us, seems to give results nearest to the truth'." (P. A. H.)]

### 13. *Gadais I.*

"In a 300 cc. beaker graduated at 50 cc., 5 g. licorice extract are dissolved in 50 cc. of boiling water, and stirred until disintegration is complete. After cooling, make up to the 50 cc. mark; 100 cc. of 95 per cent. alcohol are then added with stirring, and then allowed to stand 24 hours, covered. The liquid is poured into an evaporating dish, and when the precipitate begins to go over, it is poured on to a filter. The beaker, filter and precipitate, are washed with three portions of 15 cc. each, of dilute alcohol (two of alcohol to one of water) and the wash waters are also received in the dish. The con-

tents of the dish are evaporated to 25 cc. on the water bath. After cooling, transfer to a tared 100 cc. beaker graduated at 50 cc. Wash out the dish with water and bring the volume exactly to 50 cc. Then add 5 cc. of water which contains 1.8 cc. of 22° Be. hydrochloric acid. After stirring thoroughly, allow to stand 12 hours, so that the precipitate sticks on the bottom of the beaker. Pour off the supernatant liquid carefully, and wash the precipitate and beaker with three 10 cc. portions of water at 2° C. Add 0.5 cc. of ammonia (22° Be.,  $d = 0.922$ ) and dry to constant weight at 100°. The weight obtained, multiplied by 20, gives the percentage of glycyrrhizin, determined as the ammonium salt."

This method compares advantageously with many others on account of its exact detailed instructions. The amount of hydrochloric acid prescribed, (I prepared it exactly 22° Be. corresponding to a 34.4 per cent. HCl., and having a Sp. Gr. of 1.171) is sufficient for the precipitation. A further addition of acid did not precipitate any more glycyrrhizin. According to my experience, it is more desirable, after precipitating, to allow to stand 24 hours instead of 12, particularly when hydrochloric acid is used. Gadais seeks to achieve a purification of the precipitated acid, by decantation with three 10 cc. portions of water at 2°. I do not believe that the total hydrochloric acid is washed out by this means. Since the ammonium glycyrrhizinate, after drying, shows Beilstein's chlorine reaction, it must contain ammonium chloride weighed as ammonium glycyrrhizinate. The wash waters, when evaporated, give only a very slight precipitate with sulphuric acid, which is to be ascribed to the slight solubility of glycyrrhizic acid in cold water, and also to the fact that the water only acts on the surface of the acid for a short time. From 5 g. licorice I obtained 0.454, 0.459, 0.469, 0.476 g. which corresponds to 9.1-9.5 per cent. ammonium glycyrrhizinate. As the loss, I figured 1.4-1.6 per cent. The insoluble matter was 44 per cent.

This method is well worked out, being especially exhaustive in the instructions given. It gives practical results, except for the unavoidable errors connected with every glycyrrhizin determination.

#### 14. Gadais II.

"Ten g. licorice extract are dissolved in 100 cc. water in a vessel graduated at 100 cc. and 301 cc. After disintegration of the licorice and cooling, water is added up to the 100 cc. mark; 170 cc.

95 per cent. alcohol are then added with stirring, and then more alcohol up to the 301 mark. After thorough shaking, the contents of the flask are transferred to a conical flask, which is stoppered up, and the gums, etc. are allowed to settle for 2 hours; the clear liquid is then poured off into a vessel graduated at 150 cc. When the precipitate begins to pass over, it is filtered through a fluted filter of 19 cm. diameter, until 150 cc. filtrate is obtained. The filtrate is transferred to an evaporating dish and evaporated to 25 cc.

"The further procedure is the same as for the first method."

[TRANSLATOR'S NOTE.—Linz points out that this method is intended for rapid analysis, and saves 24 hours standing. Linz concludes that this more rapid method gives results, which hardly differ from Gadais I. (P. A. H.)]

15. *Trubeck (1900).*

"Two g. licorice are dissolved in 5 cc. water, starch and gums precipitated with 20 cc. 96 per cent. alcohol, and the residue filtered and washed with dilute alcohol (4 alcohol to 1 water) until the filtrate is colorless. The filtrate is evaporated to about 1.5 cc., the residue is dissolved in 2 cc. glacial acetic acid, and 30 cc. absolute alcohol are added with shaking. After standing to settle the precipitate, filter through a tared filter, wash with absolute alcohol until neutral, dry three hours at a 105°, and weigh. The precipitate does not consist of glycyrrhizin only, but also contains alkalis."

[TRANSLATOR'S NOTE.—Linz points out that glycyrrhizin compounds are probably precipitated with starch and gums, by the use of so much strong alcohol. Linz also points out a number of other objections, which render this method without value, and he also states that it is not possible to improve it, with a view to making it workable. (P. A. H.)]

16. *Schröder (1884).*

[TRANSLATOR'S NOTE.—This method uses repeated precipitation with sulphuric acid, but gives absolutely no details as to quantities. Linz points out that the losses from repeated precipitations are obviously very great, and that the method has only historical interest. (P. A. H.)]

*17. Müntzer (1888).*

"Ten g. licorice extract are extracted for two hours in a flask with 190 g. of water and 10 g. ammonia. After allowing to settle, pour the liquid on a filter, wash the flask, and filter with small quantities of the extraction liquid, totaling 100 cc. The filtrate is acidified with dilute sulphuric acid. After standing one hour, the precipitate is filtered, and washed with water. It is again dissolved in 5 per cent. ammonia, and again precipitated. After standing one hour it is filtered through a dry, tared filter, washed with pure water, dried at 100°, and weighed."

[TRANSLATOR'S NOTE.—Linz points out the great loss of glycyrrhizic acid, resulting from the large volume of wash water used. The re-precipitation also causes much loss of glycyrrhizin. Linz determined the losses to be nearly as much as the glycyrrhizin actually weighed. Linz rightly states that the method cannot be used as a quantitative determination. (P. A. H.)]

*18. Morpurgo.*

[TRANSLATOR'S NOTE.—This method makes use of ammonium oxalate, presumably to decompose calcium glycyrrhizinate. Linz did not check up this method, and it cannot be considered of any special value. (P. A. H.)]

*19. Dutch Pharmacopœia (1905).*

"Five g. licorice extract are dissolved in 50 cc. water to which 2 cc. spirits of ammonia have been added. The volume is made up to 100 cc. with water. Sixty cc. of this is filtered, and evaporated to 15 cc. After cooling, 5 cc. dilute hydrochloric acid are added. After settling, the precipitate is brought onto a filter, washed with 5 cc. water, and dissolved on the filter with ammonia. The solution is evaporated, dried in a desiccator, and weighed. The dry residue should weigh at least 0.24 g., corresponding to a minimum of 8 per cent. glycyrrhizin."

[TRANSLATOR'S NOTE.—Linz objects to the extreme difficulty of filtering the original ammoniacal solution, which objection he justly raises to all those methods which do not precipitate gums with alcohol. Linz points out that the filtration and washing of the precipitated glycyrrhizin is entirely unsatisfactory. He considers

the acid weighed, very impure. It gives a strong chlorine reaction and consequently, give results which are too high. Linz rejects this method. (P. A. H.)]

20. *Kinsey (1898).*

A mixture of 40 cc. of ammonia, 240 cc. of alchhol, and water up to 1000 cc. is used as an extraction liquid.

[TRANSLATOR'S NOTE.—Linz justly condemns this method on several grounds. The glycyrrhizin is precipitated from much too large a volume, and it is precipitated by sulphuric acid in the presence of alcohol, whereas the alcohol should obviously be removed. The use of dilute acetic acid to wash the precipitated glycyrrhizin, results in further loss, and the quantity of licorice used results in much too small a quantity of glycyrrhizin being weighed for an accurate method.

Linz concludes that Kinzey's method is without value. (P. A. H.)]

21. *Anselmino-Gilg (1911).*

[TRANSLATOR'S NOTE.—This method is adapted from that of Kremel, some of whose missing instructions are here supplied. The original solution is made with ammoniacal water. Linz points out that a considerable loss of glycyrrhizin results from washing with 50 cc. water. Linz further states "for fundamental reasons stated in the introduction I object to the use of an ammoniacal extract. From the large quantity of water used in washing, considerable errors result. There are no other objections to this method." (P. A. H.)]

22. *Stoeder (1901).*

[TRANSLATOR'S NOTE.—This method also uses ammoniacal water to dissolve the original licorice extract. Linz points out that the quantity of wash-water prescribed is far short of that necessary, resulting in ammonium chloride being mixed in with the glycyrrhizin weighed. The glycyrrhizin is also very impure on account of the original ammoniacal extraction. (P. A. H.)]

23. *Telle (1911).*

"2.5 g. licorice extract are dissolved in 20 cc. of water in a centrifuge tube, and whirled for fifteen minutes. The clear liquid is poured off, the residue is mixed with ammoniacal water (10 cc. of



1 : 9) and again whirled for fifteen minutes. The liquid is poured off again, and the residue washed by centrifuging for ten minutes with 10 cc. water. If the liquid poured off is still colored, the washing is repeated. The aqueous and ammoniacal extracts are united with the washings, and evaporated. The thick extract is transferred to a centrifuge tube, and water added to a 10 cc. mark; 25 cc. of alcohol are then added. Gums and albumens are precipitated. After centrifuging fifteen minutes, the alcoholic liquid is poured off and evaporated. The thick extract is dissolved to 50 cc. with warm water, and after cooling, 1 cc. hydrochloric acid is added with shaking. After standing twenty-four hours, the liquid is poured off, and the residue washed with small portions, totaling 25 cc., of water saturated with ether. The filtration is made carefully, so as to bring as little as possible of the precipitate on to the filter. The residue in the tube is dissolved in 1 cc. of ammonia, and poured through the same filter. The tube and filter are washed until colorless, with ammonia water (1 : 9), and the filtrate evaporated to constant weight."

[TRANSLATOR'S NOTE.—A summary of the criticisms of Linz for this method is as follows: The abstracts in the German journals contain errors so that the original had to be consulted for checking up the method. Linz finds a second washing of the ammoniacal residue necessary. He calls attention to the fact that 50 cc. is too large a volume from which to precipitate the glycyrrhizin. He approves the use of water saturated with ether, but thinks 25 cc. too much. He also approves of the time saved by the centrifuge. Linz obtained by this method 8.97-9.27 per cent. ammonium glycyrrhizinate, with losses determined at 1.6-1.82 per cent. Linz finds this method for glycyrrhizin unnecessarily inconvenient, and does not see how to improve it in this respect. (P. A. H.)]

24. *Durier (1913).*

[TRANSLATOR'S NOTE.—This method uses ammoniacal alcohol on the original licorice extract. It uses the centrifuge, and precipitates from 50 cc., with hydrochloric acid, washing the precipitate with 5 portions of 5 cc. water. A correction of 0.023 g. for losses in washing, is made when 2 g. of original licorice is used.

Linz objects to the use of ammoniacal alcohol, to the large volume of 50 cc. for precipitating glycyrrhizin, to adding 1 cc. of ammonia before such precipitation, and to the use of the prescribed quan-

tity of water for washing. He shows that the Durier solubility-correction is incorrect, and he finds the loss to be 3.3 per cent. Linz says the method cannot be recommended, the results being decidedly too low as the losses are very high. (P. A. H.)]

25. *Haffner (1899).*

"Ten g. licorice extract are treated with about 200 cc. 95 per cent. alcohol; 25 cc. normal sulphuric acid are then added, and allowed to stand several hours with shaking. Filter, and wash with strong alcohol, as long as the filtrate is colored. Treat the filtrate with a 100 cc. of water, and with ammonia, until weakly alkaline. Remove alcohol on water bath, bring the residue to a 100 cc. and acidify with dilute sulphuric acid. Settle for an hour, filter, wash the residue with 2-3 per cent. sulphuric acid, until the washings are colorless. Dry the filter in a sulphuric acid vacuum desiccator, extract with acetone two or three times on the water bath until the last extract is colorless. To the acetone extract add a suspension of barium carbonate in water and remove the acetone on the water bath, using a tall beaker. The residue is extracted with portions of hot water, totalling 200 cc. The solution of barium glycyrrhizinate, after cooling, is filtered into a 500 cc. volumetric flask which is filled to the mark.

"The total solids in 100 cc. of the above solution are determined. The glycyrrhizic acid is calculated from the barium glycyrrhizinate. The latter is evaporated with sulphuric acid, and ignited to constant weight. From the barium sulphate weighed, the barium glycyrrhizinate in the total solids residue is calculated. The higher the barium content, the purer the weighed product."

Haffner's method brings forward a number of new ideas. Above all, the alcoholic-sulphuric extraction is new and good. I have spoken of it in detail in the introduction. The purification of the precipitated acid with acetone, is also new, as is especially the determination of glycyrrhizin as a barium salt.

[TRANSLATOR'S NOTE.—Linz goes on to point out that the large amount of alcohol necessary to wash the original insoluble matter, and the difficulty of washing the precipitated acid until colorless with 2-3 per cent. sulphuric acid, involves some loss. Linz is unable to get a sharp acetone separation. Linz makes an experiment to show that, by using alcohol, instead of acetone, he obtains a greater

purification, as well as a more convenient manipulation, since the acetone causes violent bumping, when evaporated from the tall beaker. Zetsche in criticising Haffner, proposes to avoid this bumping by using barium hydrate and a large porcelain dish.

Linz points out that the clumsy and inconvenient method of Haffner will not justify itself unless his statement had been correct, *i. e.*, "The higher the barium content, the purer the glycyrrhizic acid," and Linz clearly shows experimentally, that the statement does not hold, and that other constituents of licorice, those of acid nature, will form barium salts, and so increase the result. Zetsche objects to Haffner's method of obtaining barium sulphate, and also believes that 500 cc. water are not enough to dissolve the barium glycyrrhizinate, but Linz does not support either of these objections of Zetsche. (P. A. H.)]

Linz summarizes his views of Haffner's method as follows:

"1. The method is more troublesome than others.

"2. The values are lower than one would expect, from the results of other methods.

"3. Values obtained agree well with one another.

"4. I cannot prove direct sources of error in Haffner's method, but the low yield can only be explained by the occurrence of losses during the course of the analysis.

"5. The opinion which Haffner has emphasized that the barium content of the barium glycyrrhizinate weighed is a key to the purity of the acid is probably not true. At any rate it can be experimentally proved that it is not always true."

*26. Cederberg (1907).*

"Ten g. roughly powdered licorice extract are covered with 200 cc. 95 per cent. alcohol in an Erlenmeyer flask, then 25 cc. normal sulphuric added, and digested for several hours with frequent shaking. Filter, and wash with 100 cc. of hot alcohol. To the filtrate, add half its volume of water and render ammoniacal. Remove the alcohol by evaporation to less than 100 cc. Make up to 100 cc. and add an equal volume of 20 per cent. sulphuric acid. Collect the precipitated glycyrrhizin on a filter, wash with 50 cc. 10 per cent. sulphuric acid, and dissolve on the water bath in 95 per cent. alcohol. After washing with 50 cc. warm alcohol, the filtrate is treated with half its

volume of water, saturated with potassium hydrate, and made up to 500 cc. in a volumetric flask.

"One hundred cc. of the solution are evaporated in a weighed dish, and dried to constant weight at a 110°. Another 100 cc. are precipitated hot with barium chloride, filtered, and washed on a tared filter, dried at a 110°, and weighed.

"The amount of glycyrrhizin in 2 g. licorice extract is obtained by calculating the barium sulphate to potassium sulphate, and subtracting that amount from the quantity representing the mixture of neutral potassium glycyrrhizinate and potassium sulphate, and further subtraction of 11.58 per cent. for the amount of potassium in the salt."

[TRANSLATOR'S NOTE.—Linz shows that pieces of "roughly powdered licorice extract" are not penetrated by the sulphuric-alcohol mixture even after one and a half days, or even after several hours warming. In spite of using finely powdered material, he obtained 59-60 per cent. insoluble residue. Linz further shows that considerable loss results from precipitating glycyrrhizin from the excessive volume.

Linz demonstrates that Cederberg's barium chloride precipitation is open to serious objection, and is not practical, unless modified. With the necessary modification, he obtained the results 11.59, 11.75, 11.9 per cent. glycyrrhizic acid. (P. A. H.)]

Linz continues:

"Cederberg's method is undoubtedly interesting and original. But his method requires a long time, and weighings which are not simple, and also uses more than half a liter of alcohol for every glycyrrhizin determination. The values obtained are higher than others, because he includes in the weight much impurity. In addition to this, the losses of glycyrrhizin are high, but I have been unable to establish their amount, even approximately. . . .

"Taking into account the fact that in spite of a roundabout analytical method, one obtains results which are too high on account of gross impurity of the weighed acid, and further that the losses of glycyrrhizic acid are not inconsiderable, one cannot hail Cederberg's method in the form given, as an improvement."

27. *Schmidt (Haffner), (1911).*

[TRANSLATOR'S NOTE.—Schmidt uses Haffner's mixture of alcohol-sulphuric acid in treating the original powdered licorice extract, but instead of going through the acetone treatment, and obtaining the barium salt, he weighs the precipitated glycyrrhizin directly on a tared filter after washing with dilute sulphuric and then a little water.

Linz comments on the absence of exact instructions as to quantities of sulphuric acid with which to precipitate and to wash. He obtained 9.1 and 9.4 per cent. glycyrrhizin, and appears to have little objection to the method. (P. A. H.)]

CONCLUSIONS FROM MY RESEARCHES.

As the result of my researches, I have made a table in Appendix C which summarizes the methods, and which is intended to serve in deciding the question as to which is the best method.

A large number of the methods are summarily rejected. I so classify all those determinations, which, through false analytical procedure, give results which are certainly wrong—too high or too low. Then I also reject such methods which, through inexact or erroneous directions, give results which are unreliable, and not suitable for direct comparison.

In the first class belong the method of Capin, Erikson, Trubeck, the Dutch and French Pharmacopœias.

In the second class belong Rump, Helfenberg, Kremel, Diehl, Guignard, Py, Anselmino-Gilg, Stoeder, Schröder, Müntzer, Kinzey, Durier, Schmidt-Haffner. In this second class I have placed all those methods which do not and cannot give directly reliable results when carried out exactly as the directions call for. In so doing, however, the analytical procedure on which the method is based is not in itself designated as impracticable, but only the execution of the method, so that the particular methods in this class yield practical results, after certain modifications.

Less practical are the methods of Guignard, Gadais II, Telle and Cederberg, for reasons which I have given in discussing the individual methods.

Practical results are given by the three almost identical methods of Parry, Evans' Sons, Leshner & Webb, and Houseman, and perhaps also Gadais I.

It is true that none of these methods attempt to achieve a high degree of purity of the glycyrrhizic acid weighed. Particularly in the case of Parry and Evans' Sons, is little attention given to the washing of the glycyrrhizic acid.

According to my experience with the individual methods, none of them completely fulfills the requirements which are demanded. One must, of course, leave out of account small errors which are unavoidable in a glycyrrhizin determination.

#### EXPERIMENTS TO WORK OUT A GLYCYRRHIZIN DETERMINATION.

In the hope of obtaining a purer form of glycyrrhizic acid, I have treated the precipitated, impure acid with all the organic solvents available to me. All such attempts, including those with salts of glycyrrhizin, proved to be quite impracticable. The converse method of retaining the acid and dissolving the impurities in a solvent, did not work out. I further attempted to find a glycyrrhizin salt, more particularly of a metal, which I could purify, and then decompose again, perhaps with hydrogen sulphide. These attempts were also unsuccessful.

The copper salt, of a fine green color, seemed to promise success, but after being thoroughly washed, and decomposed with hydrogen sulphide, a glycyrrhizin was obtained which was just as dirty and unattractive as before. It seems therefore that the impurities are themselves acid in character, and are in every case attached to the metal.

All these experiments, which consumed much time, proved to be impractical. It therefore seems as though one can only proceed along the lines already laid down. I believe that the object is best obtained if one starts out from the method of Diehl.

The method which I would here propose, is of course not exact. I have often emphasized, that in my opinion, accuracy is not to be achieved. It gives good results, however, inasmuch as it corrects some of Diehl's mistakes, and makes use of the experience, which has meanwhile been gained. Above all it previously purifies the glycyrrhizic acid weighed.

#### MY OWN METHOD.

Five g. licorice are treated with 50 g. distilled water with frequent shaking and slight warming, until disintegrated, and after cooling, 100 cc. 95 per cent. alcohol are added. After standing six

hours, the mixture is filtered and the insoluble matter on the filter is washed with successive small quantities of 60 per cent. alcohol, totaling 50 cc. The filtrate and washings are freed from alcohol on the water bath, and evaporated to about 30 cc. The residue is transferred to an Erlenmeyer flask, graduated at 50 cc., the dish washed out with water, and the contents of the flask made up to the mark; 5 cc. dilute sulphuric acid are added with stirring, and the mixture allowed to stand one hour at room temperature, followed by 24 hours on ice. The acid sticking to the bottom is brought quantitatively on to a filter, and washed carefully with 15 cc. of 2 per cent. sulphuric acid. The filter is then washed with 15 cc. ice cold water, saturated with ether. The filter is dried over sulphuric acid at room temperature in a vacuum desiccator, and then extracted five times successively, with 20, 20, 10, 10, 10 cc. of hot 95 per cent. alcohol in the Erlenmeyer flask. The solutions are filtered into a tared dish, the filter washed with 15 cc. hot alcohol, and the filtrate evaporated on the water bath, and the residue dried at a 100° to constant weight.

The liquid poured off from the precipitate is united with the wash waters and after neutralizing with ammonia, is evaporated to a thick syrup. This is transferred to a glass cylinder, and the evaporating dish is washed out, making up to a mark at 18 cc.; 2 cc. dilute sulphuric are added with shaking. It is allowed to stand one hour at room temperature, and 24 hours on ice. The supernatant liquid is poured off, the precipitate brought on a filter, and washed with 5 cc. 2 per cent. sulphuric acid, and 10 cc. ice-cold ether-water, drop by drop. The residue, dried in the vacuum desiccator, over sulphuric acid, is extracted with 10, 10, 5 cc. hot 95 per cent. alcohol, the extract filtered into a tared dish, the filter washed with 5 cc. hot alcohol, and the filtrate evaporated on the water bath. The amount obtained after drying is added to the portion obtained above. The sum of the two represents the total glycyrrhizic acid in 5 g. licorice extract.

In this method I have taken particular account of practical requirements. In my opinion, it is going too far to require that the insoluble residue shall be washed until colorless. This is extremely difficult. In one experiment I washed the filter with 50 cc., and since the filtrate was still colored, a further 100 cc. was poured through. These 100 cc., however, upon evaporation gave only a very slight film of light yellow color, which can have no practical influence on the result.

For the precipitation I dissolved the extract from 5 g. licorice in 50 g. water. I consider this proportion, 1 + 9, the best. If the solution is more dilute there is danger of greater losses through the solubility in more water. If one goes under this proportion, one must necessarily use more liquid for washing, which again entails more loss. I have used the purification recommended by Diehl, because it gives good results, as I have already discussed under Haffner's method. In carrying out Diehl's method, I have already mentioned that his ammonium salt is notably of lighter color than that of the impure acid. The difference is easy to see. It is also important to note that this purification does not seem to be accompanied by any loss, as happens with Haffner's method. With the quantity of alcohol I use, one does not obtain at the end of the extraction of the acid, a perfectly colorless extract. But I am satisfied that 70 cc. alcohol is sufficient, after having convinced myself that further quantities of liquid leave, after evaporation, a hardly weighable residue. This condition is accounted for, by the extraordinary coloring power of the impurities of the glycyrrhizic acid. By evaporating the alcoholic solution, and determining the glycyrrhizic acid as such, and not as a salt, I avoid the errors of many of the other methods, which convert the sulphuric or hydrochloric acid which is not washed out into ammonium salt, and thereby obtain more or less considerable losses.

I consider the determination of the glycyrrhizin in the evaporated alcoholic solution more exact and convenient than when it is weighed in a weighing bottle on a filter paper. The determination of the loss which I give, is based upon the explanation given in the introduction. I can draw upon the large number of experiments made in this connection. The sum of the two individual determinations gives the glycyrrhizin content of the licorice.

By several glycyrrhizin determinations carried out by my method, I obtained  $9.00 + 1.11 = 10.11$ ;  $9.05 + 0.93 = 9.98$ ;  $9.31 + 0.84 = 10.15$ ;  $9.4 + 0.92 = 10.32$ ;  $9.5 + 0.91 = 10.53$  per cent.

[NOTE.—This is a misprint for 10.41 per cent. (P. A. H.)]

The method proposed by me takes considerably more time than the majority of the methods hitherto published. I attain, however, by my method, relatively high values, with a considerably higher degree of purity, and have only trifling losses of glycyrrhizic acid.



# GLYCYRRHIZIC ACID DETERMINATION IN LICORICE ROOT.

In the introduction to this work I made mention of the numerous attempts to extract the glycyrrhizic acid from licorice root. There, I gave a short description of such proposals. Those researches are only qualitative in character, and make no claim of giving quantitative results. None of them are suitable for a glycyrrhizin determination, even after changing the directions. The only methods that need be mentioned here, are those of Houseman and Erikson. This small number appears, at first sight, surprising, when compared with the 27 methods available to me for glycyrrhizin determination in licorice extract. If one remembers, however, that the glycyrrhizin content in the root is definite and cannot be diminished by any outside influence, such as adulteration.

[TRANSLATOR'S NOTE.—The *powdered* root can surely be adulterated] and then remembers, on the other hand, that licorice extract is very largely adulterated, then this difference does not appear so surprising. Then also the experimental difficulties in the case of licorice root are still more unfavorable than in the case of licorice extract and this has deterred workers from being more active with this question.

In the literature, I find, in several places, statements about the glycyrrhizin content of the root:

Tschirch-Belander .....	3.0 per cent.
Sestini .....	3.3 " "
Cederberg .....	3.0 " "
Möller-Flückiger .....	7.5 " "
Realenzyklopädie .....	2.5 " "
Tschirch, Handbuch .....	5.3-7 per cent.
Houseman .....	5.9-13.24 per cent.

With the exception of Erikson and Houseman, none of them state how they arrive at these values. They appear to be more or less a matter of estimating. In earlier publications Tschirch (*Archiv der Pharmazie*, Vol. 245) states that estimates over 3 per cent. are much too high, yet in his Handbook he himself gives 5.3-7 per cent. The values which Houseman gives, reaching as high as 13.24, must of themselves arouse mistrust.

[TRANSLATOR'S NOTE.—This high value was only in one sample out of ten. The figure given was correct. (P. A. H.)]

## THE QUANTITATIVE TESTING OF THE PUBLISHED METHODS.

## 1. TSCHIRCH-ERIKSON (1910).

The method given by Tschirch-Erikson for the simultaneous determination of glycyrrhizin and of sugars in licorice root, is fundamentally the same as that already mentioned for licorice extract. In carrying it out practically, however, there are some differences. In addition to the actual method for licorice root, I wish to discuss at this place the experiments which Erikson used, from which to establish her analytical procedure. The basic thought of the method proposed by Tschirsch, I have already discussed under the methods for licorice extract, so that I can assume at this point that it is known.

The procedure for examining licorice root according to Erikson is as follows:

"I. First the glucose is determined by 15 hours standing with Fehling solution in the cold.

"II. After filtering off the precipitated cuprous oxide, the saccharose is determined by short boiling with Fehling solution, and finally,

"III. The glucuronic acid split off from the glycyrrhizin is determined in the filtrate by long boiling with Fehling solution."

This differs from the method proposed for licorice extract. In the latter case, the glycyrrhizin is first separated with sulphuric acid, and the filtrate, containing the sugars, is treated separately. In the case of the root, the order is changed, first the glucose, then saccharose, and finally the glycyrrhizic acid being determined. The reason for this change is not clear. Erikson says that "The method has been changed by conditions imposed by the material." She does not state what grounds lead to this change.

Her research is divided into four sections:

1. Preparation of the root extract.
2. Determination of glucose.
3. Determination of glucoses present as saccharose.
4. Determination of the glycyrrhizic acid.

*1. Preparation of the Extract.*

On the basis of three experimental series, Erikson proposed the following method for the preparation of the extract of the root.

"Ten g. of powdered licorice root are mixed with an equal volume of powdered glass, moistened with a little water, and allowed to

stand several hours. The mixture is then transferred to a percolator, and 50 cc. of water added, which for every 100 cc. contains three to four drops of alkali, to combine with the glycyrrhizic acid, and convert it to a soluble form. The mixture stands overnight. The liquid is then allowed to drop at 12-15 drops to the minute, adding fresh alkaline water all the time. The extraction is continued until the percolate is tasteless. The extraction takes place at 15°. At a higher temperature Erikson adds a few drops of chloroform to prevent fermentation, and the formation of mold. The extraction liquid is received in a sterile flask and made up to 200 cc."

Houseman has objected to this method, that the long standing will cause losses by enzyme action, and this objection is not without justice, because the extraction to exhaustion takes over two days. I have often observed, that aqueous extracts of licorice root decompose extraordinarily easily. I notice this in extracting large quantities of licorice root to make chemically pure glycyrrhizic acid. It would, however, be difficult to find a way of avoiding these losses.

"For the analysis, pipette off 40 cc. of the extract, add 44 cc. 90 per cent. alcohol and heat in a beaker on the water bath. The gummy substances are precipitated by the alcohol. This operation and the subsequent removal of the alcohol must be conducted as rapidly as possible, in order that the sugars may not be decomposed. After the alcohol has been completely removed, filter through a small filter, and wash thoroughly with water, uniting the washings with the filtrate."

Attention must here be called to a remarkable difference between the directions for root and for extract. Erikson says for root, that the heating and evaporation must take place as rapidly as possible, in order to avoid losses of sugar. On the contrary, she lets the corresponding licorice extract solution stand for half an hour on the water bath with alcohol.

## *2. Determination of Glucose.*

[TRANSLATOR'S NOTE.—Linz points out that Erikson only makes a single experiment, on one variety of root, to establish that the maximum amount of cuprous oxide is precipitated in 15 hours in the cold. It is remarkable that, having considered this time for maximum precipitation established, she does not use it anyway. Linz further shows that although Erikson admits that this Fehling reduc-

tion is highly sensitive to small changes in temperature, she does not specify or control such temperature accurately. Linz's proof already given for extract, that Erikson's method cannot be possibly used, applies also in the case of root and further detailed criticism is superfluous. (P. A. H.)]

I summarize my criticism as follows: The Tschirch-Erikson method for glucose determination, has the same drawbacks when applied to root, as when applied to extract. The method does not consider the secondary reactions which take place with the use of Fehling solution. The method for determining the time the Fehling solution is to act, is open to objection. The instructions for the method are inexact, and take no account of the results of her own experiments. There is no doubt that the total glucose is not determined by Erikson's method.

### 3. *Determination of Saccharose.*

[TRANSLATOR'S NOTE.—Linz shows that saccharose does not reduce Fehling solution at all, by three minutes boiling, and that the method is hopeless. (P. A. H.)]

### 4. *Determination of Glycyrrhizic Acid.*

[TRANSLATOR'S NOTE.—Linz objects to the absence of exactly specified quantities of reagents and shows that a maximum precipitation of cuprous oxide in 14 hours, simply represents a condition of equilibrium, at which no further self-reduction of Fehling solution takes place.

He is right in passing the same unfavorable judgment on this method for root as he did in the case of extract. (P. A. H.)]

### 2. HOUSEMAN (1913).

That which makes the glycyrrhizin determination more difficult in root than in licorice extract, is the act of dissolving out the glycyrrhizic acid, quantitatively. Erikson attempts to exhaust the root by percolation. There are objections to this method, even of a purely practical kind. The starch in the root swells up so much, and sometimes gives such a thick mess that no water percolates through.

Houseman has used another method. He first of all exhausts the root with 95 per cent. alcohol, and claims that there is no glycyrr-

rhizin in the extract. After having removed the resins and bitter substances by this method, he extracts with 50 per cent. alcohol, and claims that he obtains the glycyrrhizin quantitatively. In spite of this, I am not sure whether Houseman claims a quantitative yield for his method. Some parts of his research seem to speak against it. For instance, the root is only to be used after careful picking. But for quantitative methods, one should demand that not only selected pieces can be examined, but also average samples. When further, Houseman finds 0.5 per cent. glycyrrhizin in the last alcoholic extract, and considers the root thereby exhausted, without putting on a control experiment, I fail to follow him on this point.

I will now go through his method and communicate the results of my control of it.

Before use, the root is to be dried in a vacuum desiccator. The root I used contained 9.2 per cent. of moisture. After standing five days over sulphuric acid in a vacuum desiccator, the moisture content was reduced to 3.8 per cent. Ten g. of this roughly powdered root was extracted four times with 100 cc. portions of 95 per cent. alcohol. I allowed each extract to stand 24 hours with frequent shaking. Houseman does not state how much alcohol is obtained each time. I evaporated the 400 cc. of extract, and obtained a considerable residue of a brown yellow color. The portion of this residue which is soluble in warm water, gave after cooling, and acidifying with sulphuric acid, a very trifling, flocculent precipitate, and therefore contained very small traces of salts of glycyrrhizin, and probably also traces of free glycyrrhizic acid. The portion of the root which had been freed from resins and bitter substances is now treated with 50 per cent. alcohol. Here again Houseman states no quantities.

I extracted six times, with 50 cc. each, of 50 per cent. alcohol (Houseman prescribes only five times). In order to establish the quantity of extract removed each time, and thereby the progressive extraction of the root, I evaporated the extract each time, in the same tared crucible. I so obtained the amount of extract from each succeeding extraction. After standing for a half a day, the extract was poured off and another 50 cc. of alcohol added. The extraction with the two strengths of alcohol thus lasted a total of seven days.

With 50 per cent. alcohol I obtained the following quantities after evaporation:

1....	9.38	9.11	10.35
2....	7.24	6.72	6.17
3....	4.66	4.11	3.21
4....	1.52	2.39	1.89
5....	0.52	0.45	0.78
6....	0.33	0.33	0.12 and for control.
7....	0.44	1.12	0.15
<hr/>			
	23.69%	23.23%	22.67%

After I had thus proved that the powdered root had been exhausted with 50 per cent. alcohol, I digested it for three hours on the water bath, with alcohol of the same strength. The evaporated filtrate gave no glycyrrhizin reaction. It really seems then that the total glycyrrhizin is removed by the cold alcoholic extraction. Houseman gives no further information as to how the extract is to be worked up. It is, however, clear that the extract, evaporated to dryness, is to be treated by the method which he gives under licorice extract. I so proceeded, and obtained in the residues given above, 6.4 per cent., 6.1 per cent. and 6.8 per cent. glycyrrhizic acid.

Houseman only reports, as I have stated above, on the progress of his own researches, in which he used 100 g. of each kind of root, and does not state the further examination of the alcoholic extract of the glycyrrhizinate. The extract from 10 g. of root, amounting to about 2.5 g., cannot well be dissolved in 10 cc. hot water. I needed 20 cc. and used accordingly twice as much alcohol. The glycyrrhizin obtained was of a light brown color and therefore considerably purer than that obtained by any other methods for licorice extract. The impurities, which give to the glycyrrhizin from the licorice extract a nearly black color, appear in the extract only through the method of manufacture. The control of Houseman's method shows its suitability. It seems to give quantitative yields of the glycyrrhizic acid, with a high degree of purity of the latter. Substituting an extraction with alcohol for percolation with water must be regarded as a considerable improvement.

It might be recommended to use absolute alcohol for the first extraction, and add a few drops of ammonia to the total quantity used for extraction, in order to fix the free glycyrrhizic acid, and make it insoluble in absolute alcohol.

APPENDIX A AND APPENDIX B.

Four closely printed pages of literature references.

APPENDIX C.

Elaborate statement covering four pages, summarizing, in tabular form, all of the conditions and results associated with the twenty-seven methods for determining glycyrrhizin in licorice extract, which the author has discussed.

P. A. HOUSEMAN.

May, 1921.

Camden, N. J.

MacAndrews & Forbes Co.,

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STUDIES ON LICORICE ROOT AND LICORICE EXTRACT.

By PERCY A. HOUSEMAN, PH. D., F. I. C.

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PART 3.

Previous papers on this subject by the author have appeared in this JOURNAL, December, 1912, and March, 1916. The present article is published in connection with a translation which I have made of an article by Linz (*Arch. der Pharm.*, 1916, 254, 65 and 204), entitled "Comparative Researches on the Methods Proposed for the Estimation of Glycyrrhizin in Licorice Extract." This (abridged) translation appears in two instalments in this JOURNAL, June, 1921, and in this issue.

The article of Linz is so exhaustive that it merits detailed examination. Linz subjects to critical experimental examination, twenty-seven methods which have been proposed for the determination of glycyrrhizin in licorice extract, and two methods proposed for glycyrrhizin in root. Accepting what he considers the desirable features of the best methods put forward for licorice extract, Linz compiles a method of his own.

The present writer agrees with nearly all of the criticisms made by Linz. Linz points out that all of the analytical methods proposed weigh only a more or less crude glycyrrhizin. He rightly condemns the use of an ammoniacal solvent on the original licorice extract, and approves an aqueous solution, followed by the addition of alco-

hol, which not only removes starch and gums, but renders filtration easy on a material which is otherwise very inconvenient to manipulate. Of all of the acids proposed to precipitate glycyrrhizic acid, he finds sulphuric to be the best.

For his control work on the twenty-seven methods for the assay of licorice extract Linz has used the Baracco brand. It is rather surprising that he should have been satisfied to use a material which, as he states himself, was characterized by an extraordinary content of free copper, which he invariably found present, sometimes in pieces as long as 5 millimeters, weighing 0.062 grams. A product so crudely made hardly seems the most desirable for accurate analytical control work.

Linz then proceeds to the experimental control of the twenty-seven methods, and for one reason or another rejects all except three—those of Parry, Evans' Sons, and Houseman, and possibly Gadais. Linz states that the methods of Evans' Sons and myself are both modeled on that of Parry.

I wish at this place to emphatically contradict this statement. On the first page of my article in this JOURNAL, December, 1912, I clearly stated that Parry received his method from me and that the MacAndrews & Forbes Company had used it for more than twenty years. Parry published it without acknowledgment of its source, and has contributed nothing original to the quantitative determination of glycyrrhizin. If Evans' Sons derived their method from Parry, it is evident that the method I have given is practically the only original method which Linz accepts, from the twenty-seven proposed. Subsequent experience has caused some modifications in the method I use, which I shall discuss later.

Reply may here be made to minor criticisms which Linz makes of my method. Linz cannot understand why I specify evaporating the alcoholic solution of glycyrrhizin to dryness *in vacuo*, and assumes that I evaporate *in vacuo* to avoid possible decomposition of glycyrrhizin, but this is not the case. There is no danger of any decomposition of glycyrrhizin during removal of the alcohol. It is simply that I find it a quick and convenient way to completely remove and recover the alcohol, the recovery being an important matter in these days. I consider it undesirable to direct that the alcohol shall be removed by "evaporating to a syrup," or "evaporating nearly to dryness" on a water bath. Such vagueness easily permits a trace of alcohol to remain, and that would prevent complete pre-



cipitation of the glycyrrhizin by sulphuric acid. A little alcohol is rather obstinately held by the syrup, and in order to be quite safe I prefer to remove the bulk of the alcohol by distillation in a round-bottomed flask from a steam bath without vacuum, and finish just to dryness under a vacuum. Under these conditions no trouble with bumping need be experienced.

Certain other criticisms of my method by Linz will be mentioned when I come to state my present method of analysis.

Linz further says: "When Houseman states in conclusion that he weighs pure glycyrrhizin, he is grossly deceiving himself." Linz must either have had access to a poor abstract, or have made a careless translation himself at this point. In my article of 1912 I am careful to state that *crude* glycyrrhizin is weighed.

Reference must here be made to the method of Tschirch-Erikson, because of the prominence of the first author, as well as on account of the originality of the method proposed. Linz has very carefully tested Tschirch's method, which seeks to determine glycyrrhizin, glucose and saccharose successively, on the basis of their reduction of Fehling's solution. Linz confirms my own published conclusions that the method proposed by Tschirch for determining glycyrrhizin and sugars in licorice extract and in root is completely unworkable.

I cannot understand how Prof. Tschirch can have given his sanction to the publication by Erikson, of a method, upon which obviously not nearly enough work was done, and which also on theoretical grounds is quite unsound.

This is particularly unfortunate, because the name of Tschirch has caused some acceptance of his method in the literature, when it would otherwise have been refuted. I find the Tschirch-Erikson method given, for example, in a new book by Henry C. Fuller, "The Chemistry and Analysis of Drugs and Medicines," 1920, page 50. My own method is given in a later chapter in the book (pp. 408-410).

Having disposed of the methods hitherto proposed for the assay of licorice extract for glycyrrhizin, Linz then considers the methods for licorice root. He considers only two methods worth discussion—that of Tschirch-Erikson, and my own. He is forced to refute the Tschirch-Erikson method for the same reasons as apply to licorice extract, and accepts my method, stating that it gives quantitative yields of glycyrrhizic acid, with a high degree of purity of

the latter. He accepts my alcoholic extraction of the root (this JOURNAL, December, 1912, p. 542) as a considerable improvement over percolation with water.

Before summarizing my experience of the last few years in the analysis of licorice root and extract, and giving what I consider to be the best method available at this time, I shall examine the method which Linz himself proposes for licorice extract.

*The Linz Method for Determination of Glycyrrhizin in Licorice Extract.*

This method is given on page 458 of the June issue of this JOURNAL. There are no fundamental objections to it, but it is open to certain minor criticisms, which I mention:

1. Linz precipitates starch and gums with alcohol of about 65 per cent. strength, and washes with 60 per cent. alcohol. I prefer to use 75 per cent. alcohol which completely dissolves glycyrrhizin and precipitates gums more completely. Unprecipitated gums will tend to make the glycyrrhizin figure too high.

2. Linz evaporates the alcoholic solution to 30 cc. I do not consider that all of the alcohol is sure to be removed from the remaining syrup. A trace of alcohol will make the subsequent precipitation of glycyrrhizin with sulphuric acid incomplete and yield low results. I consider the alcoholic solution should be evaporated almost or just to dryness, finishing under reduced pressure if desired.

3. Linz fails to specify strength of sulphuric acid to be used in precipitating glycyrrhizin.

4. I do not think it necessary to dry the glycyrrhizin precipitate in a vacuum desiccator before dissolving it in 95 per cent. alcohol. I was unable to dissolve it from the filter paper with the quantity of alcohol prescribed by Linz.

5. Linz precipitates a second portion of glycyrrhizin from the evaporated filtrate and washings from the first (main) portion. *This is good*, but the second portion need not be weighed separately from the first portion.

I pass now to the method which I propose.

DETERMINATION OF GLYCYRRHIZIN IN LICORICE EXTRACT.

For this determination I consider that a centrifuge is practically indispensable.

Two grams of licorice extract in a 100 cc. centrifuge tube are

allowed to stand overnight with 15 cc. water at room temperature. The mass is then stirred until completely disintegrated, 15 cc. 75 per cent. (by volume) alcohol, and 53 cc. 95 per cent. alcohol are added from a burette with stirring, to precipitate the starch and gums. This gives a total mixture containing 75 per cent. (by volume) alcohol when the licorice extract contains 25 per cent. moisture. After standing not less than three hours, the tube is centrifuged for five minutes at a speed of about 1500 R. P. M. The clear solution is poured off into a flask, the sediment is stirred up with about 75 cc. 75 per cent. (by volume) alcohol, centrifuged again and the clear solution is poured off. The sediment is stirred up a second time with 75 cc. 75 per cent. alcohol, centrifuged, and the solution is again poured off. The precipitated starch and gums are washed into a tared dish, dried and weighed. The combined three liquors are evaporated just to dryness from a water bath, preferably using vacuum to finish, and recovering the alcohol. The residue in the flask is dissolved in about 10 cc. hot water, the solution filtered through a small filter paper into a centrifuge tube graduated at 30 cc., the flask and paper are washed, and the volume made to mark.

The filtrate is cooled to 15° C., and the glycyrrhizin is precipitated with 3 cc. of 10 per cent. (by weight) sulphuric acid. The tube is allowed to stand in the ice box overnight, and is then packed in cracked ice for half an hour. The tube is centrifuged for a half a minute, and the clear liquid poured off. The precipitate is stirred up with 5 cc. ice water saturated with ether, centrifuged again for half a minute, and the clear liquid poured off. The sediment is again stirred up with 5 cc. iced ether-water, centrifuged, and the clear liquid poured off as completely as possible. The tube is kept cold throughout the operation and all of the glycyrrhizin is retained in the tube. Thirty cc. of warm 95 per cent. alcohol are added to the washed glycyrrhizin in the tube. This solution is retained to be united later to the second precipitate of glycyrrhizin. To obtain this, the combined filtrate and two washings obtained as above are neutralized with ammonia, evaporated to about 5 cc., transferred to a centrifuge tube, made to 10 cc., cooled and precipitated with 2 cc. 10 per cent. sulphuric acid. After standing overnight the tube is packed in ice for half an hour, centrifuged, and the clear liquor poured off. The glycyrrhizin is stirred up with 5 cc. iced ether-water, centrifuged half a minute, and the liquor poured off. A second washing with ice cold ether-water is given, using 3 cc. The precipi-

tated glycyrrhizin is dissolved in 10 cc. warm 95 per cent. alcohol. Both portions of dissolved glycyrrhizin are then filtered through a 70 mm. No. 40 Whatman paper into a weighed glass dish. The tubes and paper are washed with warm 95 per cent. alcohol and the washings added to the dish. Two drops of 5 per cent. ammonia are added to neutralize any traces of sulphuric acid. The solution in the dish is then evaporated to dryness and the glycyrrhizin weighed, after drying at 100° C. overnight.

The glycyrrhizin weighed is fairly pure and there seems no practicable method of purifying it further, at any rate for technical-analytical purposes.

#### DETERMINATION OF GLYCYRRHIZIN IN LICORICE ROOT.

The matter of determining glycyrrhizin in root is a little different from that of the determination in extract.

In the latter case, the root has been subjected to an aqueous extraction in the factory, and most of the resins and some of the bitter principles have remained behind in the spent root, and do not therefore enter into analytical consideration to any great extent.

The process of manufacture has effected a partial separation. In the case of determining glycyrrhizin in root, *all* of the constituents of the root must be reckoned with.

It has been suggested by some investigators that the root should be extracted with water, parallel to factory procedure in making licorice extract, the solution separated from the "spent root," evaporated and precipitated with sulphuric acid.

Linz has clearly pointed out the objections to such a procedure, which are, firstly, mechanical difficulties (powdered root is difficult to percolate with water and a solution is obtained which will not filter satisfactorily), and, secondly, a very impure glycyrrhizin is obtained.

I am therefore convinced that it is highly desirable to remove starch and gums by means of alcohol, because a clean liquid is obtained for manipulation, and a purer glycyrrhizin is weighed.

The glycyrrhizin is very conveniently removed from the root by means of dilute (75 per cent. by volume) alcohol, but this strength alcohol also removes from the root some resins and bitter principles, which may contaminate the glycyrrhizin weighed, to a greater or less extent. It is therefore necessary to consider preliminary re-

removal of resins and bitter principles, followed by removal of starch and gums.

Results of comparative experiments on this subject will now be communicated.

In one of the previous papers (this JOURNAL, June, 1912, p. 542) I have already shown that cold 95 per cent. alcohol completely removes from licorice root, resins and bitter substances together with some sugars, but does not remove any glycyrrhizin, and that the glycyrrhizin may then be completely removed by 50 per cent. alcohol. Linz confirms both of these statements.

My experiments on the preliminary removal of resins and bitter substances from the root before determining the glycyrrhizin, have been repeated and extended.

For this work powdered roots passing a 40-mesh screen were used. They were dried from their normal moisture content of about 8-10 per cent. to about 1 per cent., either by warming in an oven at about 50° C. for an hour or two, or by standing in a thin layer over sulphuric acid for a day. The roots were then extracted with solvents (ether or strong alcohol) and glycyrrhizin determinations were carried out on the roots after such extractions, and compared with glycyrrhizin determinations made directly on the original roots with 75 per cent. alcohol, in a manner similar to that described in the method for licorice extract.

#### SERIES I.

##### PERCOLATION OF ROOTS WITH 95 PER CENT. ALCOHOL.

	Spanish.		Russian.		Chinese.	
95% Alcohol removed .....	9.6%		11.4%		10.4%	
60% Alcohol then removed .....	24.7%		25.3%		24.0%	
Glycyrrhizin removed by 60% Alcohol .....	10.1	9.3	12.5	12.4	11.6	10.6
Glycyrrhizin in original root by 75% Alcohol. {	11.1	10.9	13.3	14.1	10.7	12.0
	11.0	10.8	14.0	13.4	10.9	10.5

The 95 per cent alcoholic extracts, after drying, were treated with warm water. Only a minute trace of glycyrrhizin could be detected by tasting or by precipitation with sulphuric acid.

The residual root after the 60 per cent. alcoholic extraction contained no glycyrrhizin.

The direct results on original root are, on the average, somewhat higher than those on roots previously freed from resins and bitter principles.

I think there are three causes contributing to this effect:

1. Loss of a trace of glycyrrhizin in cold 95 per cent. alcohol.
2. Slight contamination of glycyrrhizin with resins and bitter principles, when those materials are not first eliminated.
3. The glycyrrhizin obtained when resins and bitter principles are first removed is inclined to be pulverulent, while that obtained from direct extraction of the root with 75 per cent. alcohol tends to adhere together in a mass. In the pulverulent form it is more subject to loss when the sulphuric acid is being washed out with ice water or ice cold water saturated with ether.

Of the three causes mentioned, I think the third has the greatest effect on the results.

#### SERIES 2.

##### EXTRACTION OF ROOTS WITH HOT ABSOLUTE ALCOHOL.

It was found very convenient to carry out these experiments in the extraction apparatus recommended by the Joint Rubber Insulation Committee (*Journ. Ind. Eng. Chem.*, January, 1914).

Extractions were also made in which 1 per cent. and 0.5 per cent. aqueous ammonia were added to the alcohol, with the thought that the ammonia might more thoroughly inhibit removal of glycyrrhizin by hot absolute alcohol, by forming the ammonium salt of glycyrrhizic acid, should any of the uncombined acid be present in the root.

It should be noted in the results below that the Spanish root was a different sample from that used in Series 1.

	Spanish.		Greek.		Russian.		Anatolian.	
	Alc. + 1%		Alc. + 1%		Alc. + 0.5%		Alc. + 0.5%	
	Alc. NH <sub>3</sub> OH		Alc. NH <sub>3</sub> OH		Alc. NH <sub>3</sub> OH		Alc. NH <sub>3</sub> OH	
Hot Abs. Alcohol ex-								
tracted .....	12.2	10.6	11.4	12.3	5.7	8.9	4.0	7.6
Glyc. after Hot Abs.								
Alcohol .....	8.1	8.2	6.4	5.9	12.1	10.3	11.0	10.1
Glyc. by direct method								
on root .....	11.5	11.2	10.2	11.6	14.1	14.5	14.3	

*Conclusions.*—The "direct" glycyrrhizins are decidedly higher than those from roots extracted with hot absolute alcohol, and yet in the alcoholic extracts only a trace of glycyrrhizin was found.

Moreover, the "direct" glycyrrhizins were only slightly less pure than the others, judging by color and taste. Here, again, it seems to be a question of the physical condition of the glycyrrhizin,—that which is obtained from root previously treated with absolute alcohol is subject to greater loss in washing than that not so treated.

This is easily shown as follows:

The glycyrrhizin method which I have given for licorice extract prescribes two precipitations with sulphuric acid—the first giving the main portion, and the second giving a supplementary portion from the evaporated filtrate and washings from the first. When, now, this procedure is carried out with root on which no preliminary treatment with strong alcohol is given, the second portion is very small (the first main portion will be, say, 10 per cent., and the second usually 0.3-0.6 per cent.). When, however, the analytical process is applied to root which *has* been treated previously with strong alcohol, the washings from the main glycyrrhizin precipitate are very noticeably of darker color, giving a much larger second precipitate, and even the filtrate and washings from the second portion sometimes contain a considerable amount of glycyrrhizin. The first portion frequently drops to, say 5 per cent. and the second-portion may be as much as 2 per cent., a clear indication of the reason for low results, viz., that glycyrrhizin has in this case been lost in the washing. The low results are not due, essentially, to removal of glycyrrhizin by the strong alcohol, and the high results in the "direct" method are not essentially due to contamination of the glycyrrhizin with resins and bitter substances.

There is no advantage in adding a little ammonia to the absolute alcohol. It renders the extraction of resins and bitter substances less sharp, and gives slightly lower glycyrrhizin figures.

The conclusions drawn from the table above were confirmed by repetition. In fact the discrepancies were even more marked.

	<i>Spanish.</i>	<i>Greek.</i>	<i>Russian.</i>	<i>Anatolian.</i>
Hot Abs. Alcohol Extract .....	11.2	8.4	10.4	8.3
Glycyrrhizin in residual root (based on original root) .....	5.8	7.4	8.9	9.8
"Direct" glycyrrhizin .....	11.1	10.4	14.1	14.7

It was easy to notice in carrying out this series, how a considerable part of the glycyrrhizin from roots previously treated with hot

absolute alcohol, was dissolved in the washing of the precipitated glycyrrhizin with ice cold ether water.

The idea of extracting the root first with hot absolute alcohol was therefore abandoned, partly because such an extraction was not at all sharp, but chiefly because it left the glycyrrhizin subsequently obtained, in such a condition that it was subject to serious loss in washing.

### SERIES 3.

#### EXTRACTION OF ROOTS WITH ETHER.

Ether removes the resins from licorice root, but not the bitter principles. The ether extraction may be carried out in the apparatus of the Joint Rubber Insulation Committee. It may also be done by simply stirring up the powdered root (about 3 grams) in a 100 cc. centrifuge tube with 75 cc. Ether U. S. P., centrifuging for a few minutes, pouring off, and giving a second and third treatment with ether. The resins are very easily dissolved out by ether.

	<i>Spanish.</i>	<i>Greek.</i>	<i>Russian.</i>	<i>Anatolian.</i>
Ether Extract .....	2.5	1.3	4.2	2.3
Glycyrrhizin in residual root (based on original root) .....	9.6	10.1	12.3	14.0
"Direct" glycyrrhizin .....	11.1	10.4	14.1	14.7

Note may here be made of a difference remarked in the course of the two sets of glycyrrhizin determinations.

My method calls for evaporation of the 75 per cent. alcoholic solutions containing the glycyrrhizin, just to dryness, followed by solution in 10 cc. hot water. In the series in which the root had been treated with ether to remove resins, complete solution of the residue from 75 per cent. alcohol, was obtained when 10 cc. of water was added. When, however, the original root is not treated with ether, complete solution is not obtained in 10 cc. water. An insoluble residue remains which was found to be soluble in ether. The "direct" method therefore of itself eliminates the resins to some extent, inasmuch as it leaves at least a part of them undissolved in water after evaporation of the solution in 75 per cent. alcohol.

Having rejected the preliminary extraction of the root with hot absolute alcohol, I have now to choose between four methods:

1. Direct treatment of root with 75 per cent. alcohol.
2. Treatment with ether, followed by 75 per cent. alcohol.



3. Treatment with cold 95 per cent. alcohol, followed by 75 per cent. alcohol.

4. Treatment with cold absolute alcohol, followed by 75 per cent. alcohol.

A new series of determinations was now made in order that the four methods could be compared simultaneously.

The Russian root in this series was a new sample, and therefore the results on this one sample are not to be compared with the earlier series.

Instead of the tedious method of percolating the powdered roots with ether, 95 per cent. alcohol and absolute alcohol, extractions were made with these solvents in centrifuge tubes. The procedure was to stir up 3 grams of the ground root with 75 cc. of the solvent for 15 minutes, centrifuge, pour off the clear liquor completely, and repeat with two more 75 cc. portions, stirring each time for 15 minutes before centrifuging. This method gives a bright liquor, which can be poured off from the root to the last drop. The amounts of extracts obtained agreed excellently with those from the slow percolation method, and the extraction is finished in little more than an hour, the last liquor being practically colorless.

#### SERIES 4.

##### COMPARISON OF FOUR METHODS.

	<i>Spanish.</i>		<i>Greek.</i>	<i>Russian.</i>		<i>Anatolian.</i>	
Ether Extract .....	2.0	2.3	2.4	3.2	3.2	2.1	2.5
Cold Absolute Alcohol Extract ..	5.5		5.0	6.5	7.2	4.7	6.7
Cold 95% Alcohol Extract .....	8.9		7.8	12.0	11.7	10.3	10.0
"Direct" Glycyrrhizin .....	11.5	11.2	11.0	12.6	13.2	14.7	14.8
Glycyrrhizin after Ether .....	10.4	10.4	10.1	10.2	10.6	13.8	14.1
Glycyrrhizin after Abs. Alcohol ..	9.0		8.9	9.6	9.8	12.9	11.1
Glycyrrhizin after 95% Alcohol ...	8.4		8.2	8.0	8.8	12.1	9.8

After extracting the various roots with ether, 95 per cent. alcohol or absolute alcohol, and then treating the residual roots in the tubes three times with 75 per cent. alcohol, the residues were extracted with a hot 5 per cent. solution of ammonia to determine whether all of the glycyrrhizin was removed.

The treatment with hot weak ammonia extracts starch and gums, but the solutions were found to contain no glycyrrhizin.

One notices very clearly that the more material removed by the preliminary extraction, the lower the value for glycyrrhizin subsequently obtained.

The most obvious explanation is not the true one. One might think that:

1. Either the preliminary solvent removed glycyrrhizin.
2. Or the glycyrrhizin was more or less contaminated with bitter substances according as they were less or more removed by the preliminary treatment.

The first possibility is easily disproved by examining the ether or alcohol extracts for glycyrrhizin. Never more than a trace is present.

The second possibility may account for a small part of the differences in the values, but judging by taste and color there can be no large amount of impurity in the glycyrrhizin obtained. The main cause of the differences, as already explained in detail, is that, the more non-glycyrrhizin removed in the preliminary treatment, the more subject to loss by washing is the glycyrrhizin, on account of being then left in a granular form rather than in a compact form which can be kneaded with the ice-cold wash-water.

In summarizing, it must be remembered that no known method weighs *pure* glycyrrhizin. We have to choose the method weighing as pure a glycyrrhizin as possible, and in which the loss in manipulation is as low as possible.

With the preliminary alcoholic extraction I feel that serious manipulative losses are difficult to avoid, and in some cases inevitable.

On the other hand I feel that a direct treatment of the root with 75 per cent. alcohol yields a glycyrrhizin which is contaminated a little more than necessary with impurities.

As the best available compromise I therefore choose an ether extraction to remove resins, followed by extraction with 75 per cent. alcohol to obtain glycyrrhizin.

The details of the method are here set forth:

#### DETERMINATION OF GLYCYRRHIZIN IN LICORICE ROOT.

The sample of ground root (it is not necessary to specify any particular degree of fineness, but it should be not coarser than 20 mesh) is dried to a moisture content of not more than 2 per cent. This is easily accomplished by allowing to stand in an oven for an hour or two at about 50° C., or by spreading out a thin layer for a day in a sulphuric acid desiccator.

Three grams of the powdered root are extracted in the Extraction Apparatus of the Joint Rubber Insulation Committee with 50 cc. Ether U. S. P. The extraction is finished in about one hour and will remove from most kinds of licorice root, 1.5 to 4.5 per cent. resins.

The residue in the thimble is dried and transferred as completely as possible to a 100 cc. centrifuge tube. The thimble is washed with 75 per cent. (by volume) alcohol and the washings poured into the centrifuge tube. The volume of 75 per cent. alcohol in the tube is made up to 75 cc. The mixture is stirred frequently and then allowed to stand overnight.

The ether extraction may also be done in a centrifuge tube by stirring for 15 minutes each time with three 75 cc. portions of ether, centrifuging and pouring off the clear liquor after each treatment. In this case there is no thimble to dry and wash, the ether being removed by placing the centrifuge tube in the oven for a few minutes; 75 cc. of 75 per cent. alcohol are then added to the root in the tube.

The subsequent treatment follows that already described for licorice extract—and comprises two further treatments with 75 per cent. alcohol, stirring for 15 minutes each time, centrifuging and pouring off the clear liquors, evaporating to dryness, dissolving in 10 cc. water, filtering up to 20 cc. (instead of 30 cc. prescribed for 2 gms. Licorice Extract), precipitating with 3 cc. 10 per cent. sulphuric acid, etc., as already described. Wash twice with ice cold water saturated with ether, using 5 cc. each time. Precipitate a second portion of glycyrrhizin by evaporating the filtrate and washings from the first portion to about 5 cc. after neutralizing with ammonia, subsequently transferring to a tube marked at 10 cc. and using 2 cc. 10 per cent.  $\text{H}_2\text{SO}_4$  for the second precipitation, and washing twice with iced ether-water as already described. The two fractions are dissolved in 30 and 10 cc. respectively of warm 95 per cent. alcohol, filtered, and united. Two drops of 5 per cent. ammonia are added to fix any trace of free sulphuric acid and the solution evaporated to dryness, dried at  $100^\circ \text{C}$ . and weighed.

There is no doubt that the figures given in the literature for glycyrrhizin in licorice root are too low.

Kraemer in his new book, "Scientific and Applied Pharmacognosy" (1920), gives a figure of "about 3 per cent." for glycyrrhizin in Russian licorice root. Tschirch in his "Handbuch der Pharma-

kognosie" gives 6.42-7.13 per cent., although in an earlier publication he speaks of 3 per cent.

The method, which I have given above, yields a glycyrrhizin more nearly approaching purity than that of any method heretofore published. The glycyrrhizin obtained by my method (ether extraction, followed by 75 per cent. alcohol) is light in color, intensely sweet, and practically free from resins and bitter principles. Yet I find figures from about 10-14 per cent., the former figure being for Spanish and Greek roots, and the latter for Anatolian, with Russian and Chinese intermediate.

Licorice extracts should contain about twice as high a percentage of glycyrrhizin as the corresponding roots, but there is no doubt that, in factory practice, a considerable loss of glycyrrhizin through hydrolytic decomposition occurs.

With regard to determining other analytical items in licorice extract and root, there is little new to add to the information contained in my earlier papers.

In root one would usually determine moisture, total ash, ash insoluble in hydrochloric acid (sand, dirt), resins (ether extract), glycyrrhizin, sugars, crude fibre, and screen analysis (on powdered roots). The sugar determination is made with Fehling solution before and after inversion, employing either the filtrate and washings from the glycyrrhizin determination, or an original portion of root, using normal lead acetate and following suitable methods given by the Association of Official Agricultural Chemists, of Washington, D. C.

Crude fibre is also done according to the A. O. A. C.

In licorice extract one may determine moisture, ash, matters insoluble in cold water and in hot water, starch and gums, glycyrrhizin and sugars.

#### *Matters Insoluble in Cold Water.*

Two grams of the licorice mass are weighed into a small copper-gauze basket, which is suspended in a 100 cc. centrifuge tube. The tube is nearly filled with cold water, and when the paste is completely disintegrated (after about 18 hours), the basket is agitated, washed and removed. The contents of the tube are whirled in an electrical centrifuge for 10 minutes at about 1500 R. P. M. The clear liquor is poured off, and the sediment stirred up with fresh water

and whirled in the centrifuge for a further 10 minutes. The liquor is again discarded and the sediment is washed into a weighed glass dish and evaporated, and the residue, dried in an oven at 100-105 °C. for 24 hours, is weighed.

*Matters Insoluble in Hot Water.*

Two grams of licorice mass are placed in a 100 cc. centrifuge tube, which is nearly filled with hot water. This is kept hot on a suitable bath and stirred at intervals until all soluble matter is in solution. The further operation is carried out as under "Matters insoluble in cold water," using hot water throughout.

*Sugars* are determined in the filtrate from the glycyrrhizin determination, or preferably on an original portion of the licorice extract, using neutral lead acetate to clarify, and following directions of the Association of Official Agricultural Chemists.

SUMMARY.

1. The method of Linz for the determination of glycyrrhizin in licorice extract is discussed.
2. A method is given for the determination of glycyrrhizin in licorice extract.
3. Comparative experiments have been made on various methods for separating part or all of the resins and bitter principles from licorice root, before proceeding to the determination of glycyrrhizin.
4. A method is given for the determination of glycyrrhizin in licorice root, involving removal of resins with ether, followed by extraction of glycyrrhizin with 75 per cent. alcohol.
5. The figures for glycyrrhizin in licorice root, published by other investigators, and in books, are too low.
6. The other constituents of licorice extract and root, which may be advantageously included in an analysis, are mentioned.

I have been very ably assisted in this work by Messrs. Bertrand Schneeberg and Milton Hartman, and express my thanks to them, as well as to the MacAndrews & Forbes Company, which has generously encouraged the work.

LABORATORY OF THE MACANDREWS & FORBES COMPANY,

Camden, New Jersey.

June 17, 1921.

SOUR SALT, A NEW SYNONYM FOR TARTARIC ACID  
OR CITRIC ACID.\*

By CHARLES H. LAWALL, PH. M.

During the year 1920 the Pure Food Bureau of the Pennsylvania Department of Agriculture received a number of complaints from customers of small groceries and delicatessen shops, particularly in the sections where Jewish inhabitants predominated. These complaints were concerned with the alleged adulteration of a substance known as "sour salt," which was purchased either in bulk or in small cartons under that name and was used to reinforce vinegar in giving acidity to certain foods, particularly to sour soups.

Upon investigation it was found that some of the firms selling the product in cartons were labeling it "sour salt" and also "tartaric acid" on the other side of the carton. The substance is always found in crystal form when sold under this name.

When samples were taken from the stores concerning which complaints were received it was found upon analysis that the product, instead of consisting of tartaric acid, or citric acid, as is supplied in some localities, was composed wholly or in great part, of alum crystals.

As alum is specifically prohibited by the food laws of Pennsylvania for sale or use in foods there was no difficulty in obtaining convictions in the majority of the cases which were instituted, for adulteration under the Food Act.

In one case, however, the defendant (a wholesaler) escaped conviction by perjuring himself to the effect that he had purchased the mixture of tartaric acid and alum crystals from several large chemical manufacturers, under the name "tartaric compound," and that he did not know that it contained alum. After his acquittal the matter was taken up with the manufacturers named, in order to learn the facts in the case, and it was shown that the defendant had been purchasing tartaric acid and alum separately, in original containers and was undoubtedly doing the mixing himself.

Some time subsequent to this investigation the Bureau of Chemistry of the U. S. Department of Agriculture issued a "Service and Regulatory Announcement" covering the subject, as follows:

\* Read at a meeting of the Penna. Pharm. Assoc., June, 1921.

"353—SOUR SALT.

"Investigation has shown that under the name 'sour salt,' purchasers expect to receive an article consisting of tartaric acid, or citric acid, or a mixture of both.

"A product containing alum, labeled as sour salt is regarded as both adulterated and misbranded under the Food and Drugs Act."

This is an interesting example of the birth of a new synonym. for a careful search of the literature of pharmacy or even of general reference works has failed to show any record of the synonym having been recorded. Although synonyms are usually misleading and unreliable, this one will have to be noted and observed, because of the official sanction which it has received from an important bureau of the government at Washington.

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SOME NOTES ON THE ASTRINGENCIES OF RED ROSE  
AND PALE ROSE.\*

By JOSIAH C. AND BERTHA L. DEG. PEACOCK.

Last year a paper entitled "The Tannin of Red Rose" was read before this body. In it were discussed the properties of that astringent principle with the result that characteristic differences from other known astringent principles were shown.

Because of the interesting features of this constituent of Red Rose an examination of Pale Rose was undertaken for report to this meeting.

Concerning the presence of a "tannin" in Pale Rose there seems to have been doubt, for, though some authors state positively its existence in small amounts, Maisch, in his "Manual of Organic Materia Medica," 1892, gives as constituents: "Little volatile oil, mucilage, sugar, tannin (quercitrin?), malates, etc." Certain it is that the matter had not attracted the necessary attention to decide this question.

It is very natural to base one's inference regarding the presence and relative amount of "tannin" on the simple test of taste, as mentioned last year, when it was pointed out that the astringency and bitterness of Red Rose are experienced simultaneously and are

\* Read at a meeting of the Penna. Pharm. Assoc., June, 1921.

about equally pronounced. This description, however, does not apply to Pale Rose, which is strikingly bitter rather than astringent.

It is desirable, for the sake of a proper understanding, to state at once that "the tannin of red rose" is present in Pale Rose as well, but in a very much less proportion.

A fair impression of this amount may be gathered from the fact that a kilo of Pale Rose did not yield sufficient to permit of the "tannin" being entirely separated from adhering matter, while the same weight of Red Rose gave an abundant sample of the purified principle.

In the case of Pale Rose, as in Red Rose, the presence and close association of much larger amounts of the "quercitrin" of other observers makes the isolation of the astringent principle both tedious and wasteful.

For a proper comparison of the following notes on Pale Rose, reference should be had to the article of last year on Red Rose.

When Pale Rose was boiled with successive portions of water, the reddish color of the material and the bitterness were entirely removed, and they failed to reappear upon subsequent drying of the undissolved portion. The infusion was feebly acid to litmus. While the first impression made by this infusion on taste was of bitterness, the last was plainly of astringency. Diluted sulphuric acid developed a reddish color and a distinct opalescence in the infusion. Upon boiling, a precipitate of burr-like aggregates was formed, identical in appearance and properties with those obtained through like treatment of Red Rose.

Except for the much smaller proportion of astringency and the relatively greater bitterness, the physical properties of the infusions of the two roses were found to be very similar, while behavior toward reagents further demonstrated a similarity of ingredients. For instance, from the infusion of Pale Rose, as from that of Red Rose, hide powder removed all astringency and bitterness; all acidity to litmus, and all color except a straw-yellow. The resultant fluid was changed to pink by the addition of diluted sulphuric acid.

In an attempt to isolate and purify the astringent substance, the bulk of the infusion was concentrated, cooled and shaken with acetic ether, which solvent removed the greater part of the astringent principle, as subsequently found through the failure of diluted acid to produce in this liquid the burr-like aggregates upon heating.

The recovery of the acetic ether yielded a small amount of



thick syrupy residue; it consisted of the astringent principle and the substance which others have called "quercitrin." Efforts to obtain the "tannin" in a porous condition were unsuccessful in operating upon this quantity. But it was converted into scale form by dissolving in alcohol and evaporating with heat on an enameled surface.

Although the purification was not an entire success, the material by displaying the peculiar properties of "the tannin of red rose" in its behavior toward reagents, proved its identity with that substance. Especially was this fact established by the production of the burr-like aggregates when the solution of the principle was treated, hot or cold, with diluted mineral acids.

There is every reason to believe that this astringent substance is present in both drugs, but in very much smaller quantity in Pale Rose, perhaps less than one per cent. of its weight.

As it is becoming more and more evident that astringency is not a characteristic of any one substance, no more than the property of bitterness is indicative of any single material or group of them, we question the desirability of continuing to apply to such principles (other than gallotannic acid) the names "tannic acid and tannin." Instead, as a means of obviating a possibly improper terminology, the suggestion is offered that such plant substances may well be grouped under the name of "astringents," with a prefix to indicate the source; as for example: quercastriagent, rosastringent, etc.; until they are chemically classified, and even then a name so practical as these may be preferable to an intricate one which details the chemical structure of the substance.

#### EFFECT OF MILDEW UPON RED ROSE AND PALE ROSE.

Another feature of the paper presented in 1920 was a reference to a crystalline principle which seemed to develop under the influence of mildew growth upon an unstrained infusion of Red Rose. By means of an ether extraction of these materials this substance was obtained in fine white or colorless crystals, but in very small amount.

To further study this matter, and more especially this time to confirm this behavior, about 500 grams of Red Rose were exhausted with ether to remove any pre-existent ether soluble contents.

This treatment revealed the presence of fatty and waxy con-

stituents and of a crystalline substance having the same appearance and solubilities as the one being sought.

Continuing the experiment the ether exhausted residue (unchanged in appearance) was freed of this solvent, and mixed with water into a mush, which was exposed to induce a growth of mildew.

In the course of two weeks, the surface was covered with a thick layer of mycelium. This covering was removed with as little of the Red Rose as possible, and extracted with ether; which removed but a trifle of the crystalline substance.

The mush was then strained to separate the aqueous portion, and this clarified by further straining. This liquid was a deep wine-red color, strongly acid to litmus, astringent, bitter, and decidedly musty, but still strongly suggestive of rose. Ether shaken with this fluid removed the crystalline principle, thus confirming its formation under the circumstances arranged for. From this portion of the mush, the yield was several times what ether extracted directly from the Red Rose.

It is presumable that this crystalline substance is derived from some water-soluble constituent of the rose, whether the "tannin" or not. To examine this subject, the solid portion of the mush was washed with cold water while ever color was removable; then mixed again with water and the resulting mush exposed to induce mildew as before. The development of mildew was very slow and sparse compared to its appearance and amount in the previous experiment. The watery portion was found to contain none of the crystalline principle.

The same experiments were carried out on Pale Rose with the results that a small quantity of a crystalline substance, apparently the same as that from Red Rose was directly extracted by ether; while a less amount was obtained in the experiment with mildew.

These experiments shall be repeated to determine whether the crystals will develop in the mush without the appearance of mildew.

It is within the bounds of probability that this crystalline substance is related to the astringent principle.

The solubility of this crystalline principle in chloroform distinguishes it completely from the astringent principle.

The burr-like aggregates melt when heated and sublime in crystalline form, tending to re-assume this peculiar manner of association.

## THE CENTENNIAL CELEBRATION OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

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### INCLUDING A REPORT OF THE GRADUATING EXERCISES.

The Centennial Celebration of the Philadelphia College of Pharmacy and Science, held in Philadelphia from June 12th to 15th, is of nation-wide interest; for it marked the Centennary also of Pharmaceutical Education in America. It was the occasion for a retrospect reaching back almost to the very beginning of American Pharmacy,—and for the summing up of its future possibilities.

The belief was expressed by Rear-Admiral William C. Braisted, the new President of the Philadelphia College of Pharmacy and Science, and by Dean Charles H. LaWall, as well as by other prominent educators who attended the exercises that pharmacy and medicine must eventually come together in a field of co-operation; that the profession of pharmacy, one of the oldest in history, must step forward and upward to the higher plane now occupied by the other professions.

These speakers stated more than once that this advance is at hand. In his address at the reception tendered to him in the Bellevue-Stratford Hotel, President Braisted told the graduates to do more than become just druggists.

"A pharmacist should employ much of his time in research work, so that he may fit in with the general advance in dignity and importance that is coming to pharmacy," he declared. "Each man should have in the back of his drug store a laboratory, where he could devote hours to experimentation and research, where he could test the purity of water and of milk, where he could be of assistance to the community doctor and make himself a valuable aid to the public. This work would be useful in large cities, and it would be invaluable in small centres of population, where, at present, there are no laboratories. It would be a big step toward the coming co-operation of medicine and pharmacy."

In his predictions, Dr. LaWall said to the delegates to the centennial:

"The teaching of pharmacy was inaugurated in this country one hundred years ago by the apothecaries of Philadelphia when they founded the College of Pharmacy and Science. Since then the institution has undergone many changes, as have all other branches

of education, but pharmaceutical progress has been retarded, largely because of the lack of supporting legislation in many of the States.

"After years of waiting, we may say that now we are on the verge of a great advance, and within ten years more progress will be made than has been recorded during the past half century.

"The interdependence of medicine and pharmacy was never more in evidence than at present for with the introduction of biological preparations, the physician is compelled to rely upon the pharmacist for distinctive and important scientific assistance in combating the manufacture and sale of worthless nostrums and in educating the public in hygiene and health conservation."

In connection with this development idea, it is interesting to note the splendid future that has been planned for the Philadelphia College of Pharmacy and Science. One phase of this was touched upon by President Braisted when he spoke to the graduates and alumni, to whom he was officially presented for the first time on the evening of June 14th. He said:

"My whole effort will be devoted toward making the College of Pharmacy and Science a larger and better institution. I want to help to bring about the co-operation between medicine and pharmacy. I wish, by means of this fine institution, to produce the super-pharmacist of the future.

"We are going to start next fall with an increased personnel and enlarged facilities. We must stay in our old building at 145 North Tenth Street for three or four years more, and this summer it will be renovated and improved in many ways. But the plan to secure funds with which to construct a new building has not been abandoned; it has been merely postponed.

"There are men now looking for a site in this city, and I am sure that they are going to find an extremely good one. I hope that when we do decide to locate at a certain place, the site will be given to us by citizens of Philadelphia in recognition of one of its oldest and most famous educational institutions. I am also sure that there are at least one or two wealthy men here who will come to our aid; there is no doubt in my mind that we will get all of the money that we need."

As a part of the expansion of the College it was announced during the centennial that beginning next fall, courses will be inaugurated leading to degrees of bachelor of science in pharmacy, chemistry, bacteriology and pharmacognosy. Other phases of the proposed expansion of the College were enumerated by Dr. LaWall as follows:

The conducting of a series of fifteen lectures on popular scientific subjects in the College.

The development of research service to the medical profession.

The institution of research departments, which shall aid the manufacturing interests allied to pharmacy.

The founding of laboratories for the express purpose of serving the City and State in an impartial solution of problems such as the quality of foods, the purity of drugs and chemicals and other scientific questions affecting the public welfare.

The development of pure scientific research.

The development of a public museum of drug and chemical products and pharmaceutical and chemical manufactures.

The creation of a botanical garden, particularly devoted to plants of medical and economic importance.

The proper housing of the present library of more than 20,000 volumes of scientific works.

Leaving aside the question of the significance that underlay the celebration, it was upon the face a most pronounced success. The plans for the celebration had been several months in the fruition, and as a result members of the alumni in all parts of the country had received invitations long in advance of the date set for the beginning of the exercises. It is estimated that more than one thousand of the "old grads" attended, some of them coming from points as far removed as the Pacific Coast. The events were also participated in by the two hundred and twenty-five students of the graduating class, the largest such body in the past twenty-five years.

The baccalaureate service which opened the centennial was held on Sunday afternoon, June 12th, in the Episcopal Church of St. Luke and the Epiphany, at Thirteenth and Spruce Streets. An appropriate sermon was preached there by the rector of the church, the Rev. Dr. David M. Steele.

On Monday afternoon the alumni met in a lecture room at the College and there expressed their unqualified endorsement of the selection of Admiral Braisted as President of the institution. This was especially gratifying in view of the fact that it was the first time the name of the new president had been put before the alumni since his election. After an address by the retiring president of the Alumni Association, Dr. William Duffield Robinson, an election of officers for the coming year was held, and the following men were chosen:

Russell T. Blackwood, president; Mort M. Smith, first vice-president; Ivor Griffith, second vice-president; Joseph W. England, recording secretary; William H. Gano, treasurer, and Eugene Eberle, corresponding secretary. The directors selected were: Frank R. Rohrman, F. N. Moerk, W. R. Decker, Ralph R. Foran and A. T. Hahn.

Professor E. Fullerton Cook, a member of the faculty, gave an illustrated lecture after the elections, in which he recited the history and traditions of the College from its founding at a meeting of apothecaries in Carpenters' Hall on February 23, 1821. Professor Cook had gotten together a remarkable collection of photographs for this event, including pictures of Charles Marshall, the first president of the institution; members of the major faculty, including some of the pioneers of pharmacy in this country, and many other photographs of equal interest.

In the evening, the annual banquet of the alumni, trustees and students in the graduating class was held in the auditorium of the College. The exceptional heat of the day proved no detriment to the attendance at this popular function.

The centennial day exercises were held in the ball room of the Bellevue-Stratford Hotel on Tuesday morning, June 14th. The meeting was honored by the presence of William H. Carpenter, Ph. D., Provost of Columbia University, and by S. Solis-Cohen, M. D., of Philadelphia, both of whom delivered excellent addresses.

An academic atmosphere was given to the exercises by the faculty and graduating class when they marched into the room attired in caps and gowns. Headed by the officials of the College and guests, the procession marched down through the center aisle of the room, the speakers, members of the board of trustees and faculty taking seats upon the stage, and the graduating class occupying the front seats that were reserved for them.

The meeting was called to order by President Braisted at 10:40 A. M. The invocation was then asked by Dr. C. B. Lowe. Dr. Braisted, after delivering a brief but very interesting address, introduced as the chief speaker of the morning Dr. William H. Carpenter, the Provost of his own Alma Mater, Columbia University.

Dr. Carpenter spoke upon "The Significance of Education," taking up several important phases upon the question of education. He dwelt especially upon the importance of a proper balance of mind and body in acquiring a good education, pointing out that a sound

mind and a sound body were essential factors. He also declared that while in the long run the dependence of mind upon body is not very strong, it is true that the mind dominates the body and a man with an ill-equipped body and whose mind is efficient is handicapped from the start. He defined education briefly as a knowledge of values, and after touching upon the history of education he brought out that a new age postulates a new education and that at the present time there is a demand for material results. Dr. Carpenter then drew attention to influence of the heart upon the mind and quoted the words "as a man thinketh in his heart so is he," when he stated that the well-informed mind could be used for good or evil according to the nature of the thoughts originating in the heart. He emphasized the importance of the heart being right and asserted that after all the end of all education is not to make a living, but to live.

The next speaker to be introduced by President Braisted was Dr. S. Solis-Cohen, of Philadelphia. The subject of Dr. Cohen's address was "The Relation of Pharmacy to Medicine." He opened his address with a few remarks with regard to the progress of the Philadelphia College of Pharmacy and Science, referring to the advancement that has been made by the institution and the good work that it has accomplished and stated that the penalty of well-doing is the obligation to do better. Dr. Cohen spoke of the College as an institution which is soaring to an apex or summit which has not yet been reached, nor is this summit yet in sight. He then took up, very interestingly, the history of pharmacy and medicine from their origin as a single art to their gradual separation into the two professions. In the words of Dr. Cohen, pharmacy is now a sister art to that of medicine. Dr. Cohen, in his remarks, strongly censured the excessive use of the synthetic coal tar products at the present time and declared that their abuse as home remedies is very harmful. Dr. Cohen also paid a glowing tribute to Dr. F. E. Stewart for his work in establishing proper relations between pharmacy and medicine. He closed his excellent and, at times, humorous address, by directing attention to an appreciation of the importance of the soul, stating that the mind is at its best only when in accord with the soul.

Professor Charles H. LaWall was the next speaker to address the meeting upon "The Future of the Philadelphia College of Pharmacy and Science." The Dean spoke in his usual eloquent and inspiring manner, dwelling upon the ambitions of the College and tak-

ing up in detail the plans and prospects that will no doubt have important influences upon its future development and expansion.

Professor E. Fullerton Cook then made the announcements for the balance of the day, including the assignments of the various classes to their class luncheons and reunions, after which the meeting was brought to a close.

The climax of the centennial came that night with the reception and dinner to Admiral Braisted. It was probably the most brilliant affair in the annals of the institution. The reception was held prior to the dinner, and the members of all classes of the institution lined up in the Clover Room of the hotel, each graduate bearing a placard announcing the year of his graduation.

After this ceremony, the "grads" marched into the ball room, each class in the order of its age. At the head of this procession was Samuel Gerhart, member of the Class of 1854. Last of all came the young men and women who were graduated this year. Dr. LaWall acted as toastmaster, introducing the guest of honor, Dr. Braisted, and a number of other speakers, including Dr. Robinson, who represented the Alumni Association; Major Clark, of the United States Army; Joseph W. England, who presented a résumé of College History; Dean Sturmer, who spoke on the Medico Chi merger; Mr. Christensen, of the National Board of Pharmacy; Dean Bradley, of Massachusetts, and others.

The graduation, which marked the close of the centennial celebration, was held in the Academy of Music on Wednesday morning. In addressing the graduates, Admiral Braisted impressed upon them the fact that they composed the one hundredth class of their alma mater, and advised them to achieve happiness and success in their future life by adhering to the principles of Christianity.

The other speaker of the occasion, Dr. Herbert W. Hess, Professor in the Wharton School of the University of Pennsylvania, urged that every citizen remember that their individual thinking makes or mars the nation.

Diplomas were awarded to one hundred and eighty-seven students by Admiral Braisted, and the remaining sixty-eight will receive their sheep skins on reaching legal majority, or on fully satisfying the practical experience requirement. The prize scholar was Miss Anne Goldberg, who won four prizes, including the alumni gold medal awarded each year to the student having the highest scholastic average for the year.



Degrees of master in pharmacy were conferred in absentia upon Rear-Admiral Edward Rhodes Stitt, Surgeon General of the United States Navy, and a graduate of the College, and upon Dr. Edward Kremers. The same degree was conferred upon Samuel L. Hilton and Josiah C. Peacock. Degrees of master in pharmacy in course were conferred upon Ivor Griffith, a member of the College Faculty and Editor of the AMERICAN JOURNAL OF PHARMACY, and Ellery H. Harvey, now pursuing special work in plant chemistry.

Upon Miss Florence R. M. McGarrity, a former student, was conferred the degree of doctor of pharmacy. Dr. McGarrity has been elected as a teacher of chemistry in an American college in Constantinople.

Following is a list of the graduates:

*Bachelor of Science in Pharmacy and Chemistry (B.Sc.).*

Name	Where From
Keller, Alexander George, Jr. ....	Pennsylvania
Weber, Robert Boyd .....	North Dakota

*Doctor in Pharmacy (P.D.).*

McGarrity, Florence R. M., P. C. ....	Pennsylvania
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*Pharmaceutical Chemist (Ph.C.).*

Weinstein, Samuel .....	Virginia
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*Graduate in Pharmacy (Ph.G.).*

Allen, John Wesley .....	Pennsylvania
Arnold, Alfred William .....	Pennsylvania
Bausher, George Joseph .....	Pennsylvania
Beaver, Ralph .....	Pennsylvania
Beauchamps, Eurico R. ....	Porto Rico
Bill, Howard L. ....	Pennsylvania
Boyd, Lardner Clark .....	Texas
Brill, Edward A. ....	Pennsylvania
Bruce, Edward Douglas .....	Pennsylvania
Burns, Joseph Leo .....	Pennsylvania
Caldwell, Archie Lee .....	Missouri
Chambliss, George Edward .....	Tennessee
Champaine, David .....	Pennsylvania

Name	Where From
Clewell, Rollin Earl .....	Pennsylvania
Colahan, Frank Patrick .....	Pennsylvania
Cordier, Lee Garfield .....	Ohio
Davendish, Sanford Jos. ....	Pennsylvania
Davis, Robert V. S. ....	Pennsylvania
Deans, John .....	Pennsylvania
Detweiler, H. W., Jr. ....	Pennsylvania
Devine, Thomas Joseph .....	Pennsylvania
DeVittorio, Carl Donald .....	Pennsylvania
Dixon, David Bainbridge .....	Pennsylvania
Dombrowski, Henry Jos. ....	Pennsylvania
Donovan, Walter Ephraim .....	North Dakota
Eddy, Thomas L. ....	Pennsylvania
Episcopo, Harry N. ....	New Jersey
Ewing, Charles Henry .....	Pennsylvania
Finegan, Edward Thos. ....	New Jersey
Fox, Louis .....	Pennsylvania
Fox, Ray Linaham .....	Pennsylvania
Frock, Charles Thomas .....	Pennsylvania
Funcheon, Margt. Gert. ....	Pennsylvania
Garber, Hallie Jackson .....	Pennsylvania
Gershenfeld, Herman .....	Pennsylvania
Gold, Adolph E. ....	Pennsylvania
Goldstein, Benj. M. ....	Pennsylvania
Golland, Jack Kendall .....	Pennsylvania
Goodman, Jacob .....	Pennsylvania
Green, Eli Noah .....	Pennsylvania
Gross, David .....	Pennsylvania
Haas, Earl Oren .....	Pennsylvania
Haentze, Frederick Edw. ....	Pennsylvania
Haines, Emerson Snyder .....	Pennsylvania
Hall, Frederic Compton .....	Ohio
Hamilton, S. S., Jr. ....	Pennsylvania
Handelsman, Benjamin .....	Pennsylvania
Harper, Ernest Robert .....	Pennsylvania
Harrity, Michael A. ....	Pennsylvania
Henrie, Robert R. ....	Pennsylvania
Hertzler, Gaius Bricker .....	Pennsylvania

Name	Where From
Hoffstein, Albert Herman .....	Pennsylvania
Hughes, Paul William .....	Pennsylvania
Jacob, David .....	Pennsylvania
Jacobs, Alexander H. ....	New Jersey
Jaffe, Hyman .....	Pennsylvania
Jaffe, Max .....	Pennsylvania
Johnson, Sidney .....	Pennsylvania
Juresco, Samuel .....	Pennsylvania
Kane, Joseph Thomas .....	Pennsylvania
Katz, Ray Parris .....	Pennsylvania
Kearney, Francis Joseph .....	Pennsylvania
Kellam, Warrington E. ....	Pennsylvania
Kepner, Russell Albert .....	Pennsylvania
King, Raymond Wesley .....	Missouri
Kinney, John Francis .....	Pennsylvania
Klein, Louis .....	Pennsylvania
Klonoski, E. J. ....	Pennsylvania
Kreider, Obed Emmert .....	Pennsylvania
Kutcher, Maurice Richard .....	Pennsylvania
Lapayowker, Adolph .....	Pennsylvania
Lehman, Anna Isabel .....	Pennsylvania
Lerman, Benjamin .....	Pennsylvania
Lieber, Maurice L. ....	Pennsylvania
Lynn, Carl Harold .....	Pennsylvania
McCoubrie, John Hubert .....	New Jersey
McGarr, William James .....	Pennsylvania
McVey, Vane Howard .....	Wisconsin
Meier, Virginia A. P. ....	Pennsylvania
Meissner, Robert Meyen .....	Indiana
Mest, Girard Stephen .....	Pennsylvania
Miraldi, Valdo Antonio .....	Pennsylvania
Mokes, Albert Bert .....	Pennsylvania
Mowrer, William Taylor .....	Pennsylvania
Myerson, Myer .....	Pennsylvania
Nelson, Augustus W. ....	N. Carolina
Norton, Allison Sheeler .....	Pennsylvania
Novak, Edward Andrew .....	Pennsylvania
Noveck, Morris .....	Pennsylvania
Nyhart, Natalie Neita .....	Pennsylvania

Name	Where From
O'Connor, William Jas. ....	Pennsylvania
O'Mara, John Aloysius ....	Pennsylvania
Olsen, Olaf J. ....	New Jersey
Pentz, Fletcher Orville ....	New Jersey
Point Leonare Joseph ....	Pennsylvania
Potts, Milton George ....	Pennsylvania
Powell, Alfred Leon ....	Pennsylvania
Puhlick, Theodore J. ....	Pennsylvania
Randolph, Coleman L. ....	Missouri
Reinard, William Ray ....	Pennsylvania
Reynolds, Ralph Eli ....	Maryland
Rosenfeld, S. W. ....	Pennsylvania
Schneider, Karl ....	Pennsylvania
Schor, Morris ....	Pennsylvania
Schwartz, David M. ....	Pennsylvania
Shoemaker, Wm. Guy ....	Pennsylvania
Shuman, Morris ....	Pennsylvania
Singer, Irvin ....	Pennsylvania
Sless, Ephraim Gershin ....	Pennsylvania
Smith, Amos Clark ....	New Jersey
Smith, Winfield F. ....	Pennsylvania
Snively, Fred Hege ....	Pennsylvania
Solorzano, Porfirio ....	Bermudez
Solot, Louis J. ....	Pennsylvania
Sorber, Russell R. ....	Pennsylvania
Spangler, Luther E. ....	Pennsylvania
Stark, Louis ....	Pennsylvania
Starkey, Thomas Earl ....	New Jersey
Stein, Bessie ....	Pennsylvania
Steinberg, Samuel S. ....	Pennsylvania
Stief, Bernard H. ....	Pennsylvania
Stouffer, Chester Beals ....	Pennsylvania
Stout, Lynn Francis ....	Pennsylvania
Streen, Paul ....	New Jersey
Suconick, Max Herbert ....	Pennsylvania
Teah, Philip Ash ....	Pennsylvania
Tobachnick, Pauline ....	Pennsylvania
Tobachnick, Samuel ....	Pennsylvania

Name	Where From
Train, H. Jane .....	Pennsylvania
Wagner, Vernon Wilbert .....	Pennsylvania
Wagaman, Emmet E. ....	Pennsylvania
Weaner, Howard H. ....	Pennsylvania
Weinberg, Reba .....	Pennsylvania
Weinstein, Leah .....	Pennsylvania
Weiss, Joseph F. ....	Pennsylvania
White, Edward R., Jr. ....	Maryland
Winslow, Frank T. ....	New Jersey
Wisman, Maynard G. ....	Pennsylvania
Zacharias, Dixon Scott .....	Pennsylvania
Zahn, Joseph Emerson .....	Pennsylvania
Zimskind, Joshua N. ....	New Jersey
Zucker, Wm. Meyer .....	Pennsylvania

*Students Who Have Completed the Scholastic Requirements of the Course and Who Will Receive Their Diploma Upon Reaching Their Majority.*

Name	Where From
Althouse, Harry .....	Pennsylvania
Bitner, Richard Mathias .....	Pennsylvania
Connor, Edwin John .....	Pennsylvania
Freedman, Jacob .....	Pennsylvania
Gorgas, Thos. A., Jr. ....	Pennsylvania
Heffner, Edgar F., Jr. ....	Pennsylvania
Hodnett, Walter Reuben .....	Pennsylvania
Killen, William H. ....	Pennsylvania
Lipsky, Benjamin .....	Pennsylvania
Lissy, Joseph Myer .....	Pennsylvania
Pines, Charles Clifton .....	Pennsylvania
Rhoads, Lemuel Gilbert .....	Pennsylvania
Roeder, Paul S. ....	Pennsylvania
Shechter, Edward .....	Pennsylvania
Snyder, Louis Elliott .....	Pennsylvania
Staub, Brown Charles .....	Pennsylvania
Tunitsky, Samuel M. ....	Pennsylvania
Von Stanley, Eugene .....	New Jersey
Wolf, Sylvia Julia .....	Pennsylvania
Yohe, Harold Reon .....	Pennsylvania

*Students Who Have Completed the Scholastic Requirements of the Course and Who Will Be Eligible for the Degree of Graduate in Pharmacy When Other Graduation Requirements Shall Have Been Met.*

Name	Where From
Adams, Howard Ruby .....	Pennsylvania
Arkans, Morris .....	Pennsylvania
Askin, Martin .....	Pennsylvania
Belov, Abraham .....	Pennsylvania
Bernholz, Ida .....	Pennsylvania
Bernstein, Abe Meyer .....	Pennsylvania
Brown, Sara .....	New Jersey
Calvert, Ralph L. ....	Pennsylvania
Cardamone, Michael J. ....	Pennsylvania
Carlisle, Mildred F. ....	Pennsylvania
Cawley, Ellen .....	Pennsylvania
Coult, Sam .....	New York
Detwiler, David R. ....	Pennsylvania
Dyen, David Leonard .....	Pennsylvania
Eby, Wilmer Morrison .....	Pennsylvania
Fox, Sereck Hall .....	Pennsylvania
Goldberg, Anne .....	Pennsylvania
Griesing, Sterling Myers .....	Pennsylvania
Groff, Wm. Shakespeare .....	Pennsylvania
Gross, William Henry .....	Pennsylvania
Hetrich, Martin Luther .....	Pennsylvania
Hubbard, Gerald DeVon .....	Pennsylvania
Kauffman, Israel Harry .....	Pennsylvania
Keesal, Sarah .....	Pennsylvania
Korost, Leonard A. ....	Pennsylvania
Lieberman, Anna .....	Pennsylvania
Lipschultz, Maxwell E. ....	Pennsylvania
McCandless, J. P., Jr. ....	Pennsylvania
McFadden, Thos. J. ....	Pennsylvania
Marsteller, Harold W. ....	Pennsylvania
Mattern, Russell K. ....	Pennsylvania
Moyer, Ella Louise .....	Pennsylvania
Padgette, Elizabeth D. ....	Pennsylvania
Palomeque Eduardo .....	Mexico

Name	Where From
Paul, John Leroy .....	Pennsylvania
Paxson, George W. ....	Pennsylvania
Rabinowitz, Morris .....	Pennsylvania
Rapp, Ernest K. D. ....	Pennsylvania
Rosen, David .....	Pennsylvania
Rosenfield, Albert Wm. ....	New Jersey
Russell, Miriam Fay .....	Pennsylvania
Solorzano, Porfirio .....	Nicaragua
Specter, Simon Louis .....	Pennsylvania
Stagmer, Robert Irving .....	New Jersey
Staub, Luther Slifer .....	Pennsylvania
Stoner, John David .....	Pennsylvania
Young, Elvin Chester .....	Pennsylvania
Ramanuskas, Peter Paul .....	Pennsylvania

*Certificate of Proficiency in Chemistry.*

Abrahams, Harold Justin .....	Pennsylvania
Dinger, Allen LeRoy .....	Pennsylvania
McNerney, Frank M. ....	Delaware

*Certificate in Bacteriology.*

Bern, Morris .....	Pennsylvania
Conold, Clarence Carl .....	Ohio
Crenshaw, Katharine H. ....	Pennsylvania
Hoffstein, Esther S. ....	Pennsylvania
Koller, William Sides .....	Pennsylvania
Kreider, Obed Emmert .....	Pennsylvania
Lamm, Jasper Herman .....	N. Carolina
Lutz, Wilbur P. ....	Pennsylvania
MacMahon, Francis J. ....	Pennsylvania
Moody, Fred Leroy .....	Pennsylvania
Patterson, George W., Jr. ....	Pennsylvania
Stephens, Sylvia Fay .....	Pennsylvania
Vaile, Thomas .....	Missouri

*Certificate in Clinical Chemistry.*

Bern, Morris .....	Pennsylvania
Crenshaw, Katharine H. ....	Pennsylvania
Hoffstein, Esther .....	Pennsylvania

Name	Where From
Guest, Warren R. ....	New Jersey
Koller, William Sides ....	Pennsylvania
Kreider, Obed Emmert ....	Pennsylvania
Lamm, Jasper Herman ....	N. Carolina
Lutz, Wilbur P. ....	Pennsylvania
MacMahon, Francis J. ....	Pennsylvania
Patterson, Geo. Wm., Jr. ....	Pennsylvania
Sholl, Walter Douglas ....	Pennsylvania

*Certificate in Cosmetics and Perfumes.*

Gryning, John F. ....	Pennsylvania
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*Certificate in Physiological Assaying.*

Butts, Donald Chas. A. ....	Pennsylvania
Bright, Charles A. ....	Pennsylvania
Henrie, Robert R. ....	Pennsylvania
Lieber, Maurice Lewis ....	Pennsylvania
Miller, George Alvin ....	New Jersey
Palomeque, Eduardo ....	Mexico
Shechter, Edward ....	Pennsylvania
Sless, Ephraim G. ....	Pennsylvania
Sharadin, Ralph ....	Pennsylvania

*Certificate in Advanced Commercial Training.*

Martin, Frederick A. ....	Pennsylvania
Rupp, Paul Frederick ....	Ohio
Zeisig, Harry C. ....	Pennsylvania

*Countries and States Represented.*

Pennsylvania .....	196
North Dakota .....	2
Virginia .....	1
Porto Rico .....	1
Texas .....	1
Missouri .....	4
Tennessee .....	1
Ohio .....	4
New Jersey .....	18



Name	Where From
Wisconsin .....	1
Indiana .....	1
North Carolina .....	2
Maryland .....	2
Mexico .....	1
Nicaragua .....	1
Delaware .....	1
New York .....	1
Total .....	238

## ABSTRACTED AND REPRINTED ARTICLES

### STANDARDIZATION OF ADRENALIN.\*

An extremely interesting paper on the necessity of the physiological standardization of adrenalin, and of preparations of the suprarenal gland, was presented by M. M. Tiffeneau at a recent meeting of the Society of Pharmacy of Paris. M. Tiffeneau commenced by stating that of recent years adrenalins of varying degrees of purity had been placed on the market, and that he had had occasion to analyze products containing 40 and as much as 60 per cent. of foreign bodies, mostly consisting of ammonium-magnesium phosphate. M. Gérard, chief of the therapeutic laboratory of the faculty of medicine, even found a preparation, sold under the name of adrenalin, which contained no trace whatever of the active principle of the suprarenal, and was devoid of any specific action. On the other hand, he had met with adrenalins which, while proving to be chemically pure, exhibited only one-half of the physiological action of the official product. These proved to be synthetic products, representing the racemic form of adrenalin. This variation in activity, and the fact that substitutes are offered in the place of the official product, apart from its adulteration, render it imperative to establish a strict method of physiological standardization for this important remedy, as it is

\*Reprinted from *Chemist and Druggist*, May, 1921.

only by this means that its efficacy can be established. Detailing his ten years' experience in handling adrenalin and preparations of the suprarenal gland, M. Tiffeneau described his researches, and the methods adopted for the evaluation of these products. The most reliable method of establishing the physiological activity of adrenalin consists in comparing in the same animal the variations in the arterial blood pressure produced by injections of these products. An adrenalin of absolute purity and full activity is used as the standard. For these tests the dog is found most suitable, and the animal is first anæsthetised and then given an injection of atropine sulphate in the proportion of one milligram for every kilogram of body weight. Without entering into the details of the test, minutely described by the author, it may be stated that it is based, first of all, upon establishing by a series of tentative injections of a 1:10,000 solution of the standard adrenalin the most convenient increase in blood pressure produced, which is 6 cm. to 8 cm., corresponding to an increase of pressure of 12 cm. to 16 cm. of mercury. It was generally found that this was effected by a dose varying between 2/100 and 6/100 of a milligram of standard adrenalin. As a result of his exhaustive researches, M. Tiffeneau was able to establish that natural lævogyrate adrenalin possesses a vasoconstrictive action which is more than double that of the racemic (synthetic) product, the exact relationship being  $1 = 0.46$ , and from this may be inferred the dangers attending the use of a product not possessing the full activity of the official substance, particularly in the case of so active a drug. In describing his investigations on various preparations of the suprarenal glands, in the form of a desiccated powder, and as extracts of the glands, the author stated that he had established that one kilo. of fresh suprarenal gland obtained from horses contained on an average 2 grams of adrenalin. Since the loss incurred in desiccation and by removing the fat amounts to about 80 per cent., it follows that 100 grams of desiccated suprarenal gland corresponds to 500 grams of fresh gland (of horses), and contains 1 gram of adrenalin, the standard also adopted by the United States Pharmacopœia. With one exception, the commercial products complied with this standard, and, indeed, some samples examined showed a slightly higher content of adrenalin. Of interest is the observation that if carelessly stored—*i. e.*, kept in imperfectly closed bottles and exposed to light—desiccated preparations of the suprarenal gland at the end of a year show a loss of about 50 per cent. of their original content of adrena-

lin. While the desiccated preparations of the suprarenal gland were found to contain the correct proportion of adrenalin; this, the author stated, did not apply in the case of preparations obtained by extracting the glands, whether intended for injection or not, and none of the commercial samples of this class of suprarenal preparations contained the amount of adrenalin which should have been normally present. This he ascribes principally to the lack of sufficient precautions in carrying out the various manipulations entailed in extracting the glands, especially to the use of a solvent not sufficiently acid to dissolve the adrenalin in the glands. Finally, M. Tiffeneau urged the need for establishing the standard chemical tests for the evaluation of each of the various organo-therapeutic products used in medicine, and, in the absence of a satisfactory chemical test, of ascertaining a reliable method of physiological assay. Should it be found that these means are inadequate, he submitted that the manufacture of this class of products should be placed under efficient supervision by controlling the various stages in the process of manufacture, or that such establishments should be licensed.

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#### BRAZILIAN BATIPUTA BERRIES.\*

By CONSUL C. R. CAMERON, Pernambuco.

Batiputa berries are the product of the sandy, rolling, coastal regions of the States of Parahyba do Norte, Rio Grande do Norte, and Pernambuco, Brazil, where they are prized for their oil, which is said to be equal to the best olive oil and is used for about the same purposes as the latter, having both food and medicinal value. Batiputa berries are of two varieties, wild and domestic. Wild plants are said to average about 100 to the acre, but the distribution is very irregular, being dependent upon natural seeding. The shrubs are only 7 or 8 feet high, however, so that they would doubtless flourish if planted as close as 10 feet apart, or, say, 400 or more to the acre.

Probably most of the land on which the batiputa shrub is found is owned by the State governments, but considerable tracts have come into private possession, and these are generally valued at from \$1 to \$10 per acre. Public lands, however, may usually be obtained by

\*Reprinted from *Commerce Reports*, June, 1921.

any one of three ways, namely, homesteading, outright purchase, or a kind of ground rental called *aforamento*.

The *batiputa* lands are fairly well provided with transportation facilities. Part of the area is near the lines of the Great Western of Brazil Railway Company (Ltd.), or the Central Railway of Rio Grande do Norte, and a considerable part of the remainder is accessible by automobile and light truck, but pack mules and horses continue to furnish the standard means of transportation in the interior.

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## NEWS ITEMS AND PERSONAL NOTES

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SEVENTH ANNUAL EXPOSITION OF CHEMICAL INDUSTRIES TO BE HELD AT NEW YORK.—Every State in the Union will be represented at the Seventh National Exposition of Chemical Industries, which will be held in the Eighth Coast Artillery Armory, Jerome Avenue and Kingsbridge Road, New York City, during the week of September 12th. This is assured by the early list of those that have already secured space, and from the outlook the display this year will be far more important than its predecessors. One phase of the situation that is giving Managers Fred W. Payne and Charles F. Roth no little difficulty is finding room for the many new concerns that want to exhibit. Already more than 400 applications for space have been made and there is no doubt but that last year's record of 457 exhibitors will be eclipsed.

This year's exposition will be more international in aspect than any of the six preceding it for the reason that it will follow immediately after the convocations of chemists from all parts of the world that will be held in New York City early in September.

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THE HOROVITZ BIOCHEMIC LABORATORIES.—The Horovitz Biochemic Laboratories announce the opening of their new manufacturing laboratories at 220 East Fourth Street, Cincinnati, Ohio. Dr. A. S. Horovitz will personally supervise the manufacture of the firm's products.

JOSIAH C. PEACOCK ELECTED PRESIDENT OF PENNSYLVANIA PHARMACEUTICAL ASSOCIATION.—Josiah C. Peacock, of Philadelphia, was the unanimous choice for president, while Buena Vista Spring was chosen after a friendly contest as the place for holding the forty-fifth annual meeting, June 20, 21 and 22, 1922.

President Peacock is a member of the Class of '91, Philadelphia College of Pharmacy and Science, a trustee of that institution, and is chairman of the Centennial Committee on College Membership.

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## BOOK REVIEWS

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"CHEMICAL REACTIONS AND THEIR EQUATIONS." By INGO W. D. HACKH. PH. C., A. B., Professor of Biochemistry, College of Physicians and Surgeons, San Francisco. P. Blakiston's Son & Company, Philadelphia; 138 pages \$1.75 net.

The object of this book is "to supply students with necessary material and to expound the general principles of balancing equations," the author having observed that "the inability to balance a chemical equation is a most common difficulty of students of chemistry. It does not enter into a detailed discussion of physico-chemical equations, but confines itself to a consideration of purely chemical equations from a technical and arithmetical standpoint."

Chapter I deals with Symbols and their use in expressing atoms, molecules and ions; Chapter II with Formulas of various kinds (empirical, rational, etc.), Valence and Valence Numbers, Oxidation and Reduction; Chapter III with Equations involving no Oxidation and Reduction; Chapter IV with Equations involving Oxidation and Reduction; Chapter V with Reactions and their Control; Chapter VI with Types of Chemical Reactions and Equations.

Reactions are illustrated with both molecular and ionic equations, and the methods used in balancing them. Under Control are considered the influence of temperature, surface, catalysts, concentration, etc. Each chapter closes with a rather comprehensive set of questions and problems bearing upon or illustrating the matter therein, adding materially to the value of the book as a student's companion.

Following the six chapters mentioned are to be found: Appendix I, Key to Nomenclature of Chemical Compounds; Appendix II, Displacement Series; Appendix III, The Periodic System and Classification of the Elements; Appendix IV, Solubility Table of Compounds; Appendix V, Preparation of Salts and Key to Equations, and, finally, a very useful Index and Glossary.

The type and composition of the book are satisfactory and the language clear and concise, but the volume shows numerous evidences of the lack of the careful proof reading that should be given all text-books, and particularly those in which much of the text is in the form of formulas or equations in which every letter, figure and other character counts for so much.

The reviewer unhesitatingly recommends the book to any person who desires a clear, compact treatise on equation writing.

F. P. S.

# THE AMERICAN JOURNAL OF PHARMACY

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No. 8.

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## EDITORIAL

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### THE COMPULSORY ADOPTION OF THE METRIC SYSTEM.

There is a needless hue and cry in the air over the compulsory introduction of the Metric System into general commercial use in this country. A bill known as The Metric Standards Bill has been introduced into Congress which calls for the forced adoption of this system. Provision is made in this bill for the gradual advance to the decimal metric units of weight and measure during a transitional period of ten years. It also enables the manufacturer to choose any weights and measures for use in production, but calls for the exclusive use of the Metric System in commercial transactions. All the organizations in favor of its compulsory adoption have combined forces and under the designation "The World Metric Standardization Council" are conducting a forceful campaign to influence the country at large to accept this system as the recognized standard of weights and measures. This Council has met some bitter opposition from another aggregate of organizations who predict disastrous results to business if the country is to be forcibly made to adopt this Metric System plan. This latter organization is termed "The American Institute of Weights and Measures," and its campaign of education, if it might be so termed, is intensive, expensive, and quite as forcefully conducted as that of its opponents. Both sides marshal an imposing array of arguments and a formidable army of proponents, and, if judgment were to be based purely upon the presentation of the issues by these organizations of *pros* and *cons*, it would be indeed a difficult task to choose sides in the argument.

The multiplicity of arguments with which we have been literally

overwhelmed by both sides in this controversy have almost biased our opinions and we hesitate to offer our judgment at this time, lest it be not candid and lucid. We are tempted, however, to submit in detail some of the demonstrations which both sides have presented to the country in their most recent communications. Pharmacists need to ponder carefully over these various considerations before formulating their judgment. The fact that this system lends itself remarkably well in serving certain phases of our activities and practices must not blind our judgment insofar as to favor its compulsory adoption by all the people and all the industries. The guiding motive of those who seek to offer opinions on this all-important subject must be based on a desire to serve not a single branch of industry or service, but rather with an eye to conveying an improvement that will benefit the great majority of industries and services.

Academicians have been too prone to ridicule the cumbersome old English systems of weights and measures with their alleged ponderous and conflicting units and they have been frequently and properly criticized for having obscured in the ardor of their decimal enthusiasm certain marked advantages which these systems exhibit. We never recall that our metric arithmetic teacher ever pointed out to us the labor saving which results from the use of the dual or duodecimal systems; that five is the only digit under seven which is not divisible into twelve, while two and five are the only two which divide into ten; that ten is not expressible in integral units when divided into quarters or thirds the latter fraction running into rows of integers that recur into Einsteinian endlessness. These advantages, of course, are well balanced when the metric simplicity is considered, and our coinage system is proof positive of the ease with which *ten* lends itself to our everyday arithmetical processes.

Rather than elaborate further on the matter the arguments herewith are presented, culled as they are from various sources, in order to afford a résumé of both sides of the question.

### *Arguments for the Adoption of the Metric System.*

Under the metric system only three names are used.

- (1) The *meter* and its decimal values for measures of length.
- (2) The *litre* and its decimal values for measures of capacity.
- (3) The *gram* and its decimal values for measures of weight.



These three units are simply related, *e. g.*, for all practical purposes, 1 cubic decimeter equals 1 litre and 1 litre of water weighs 1 kilogram.

Exclusive use of the metric system is in force in France, Italy, Germany, and thirty-one other countries.

Even the most rabid opponents of the metric system admit that the metric system is simple and easy to use, but they always fall back on their "bugaboo argument" that the compulsory change to metrics will involve tremendous expense in installing new machines, etc.

There is little basis for this contention, and it has been disproved so often by the very men who should know, namely by captains of industry, that we are forced to the conclusion that the opponents of the metric system simply haven't given the matter any thought and are ignorant of the manner in which the metric system can be operated.

There is no need for manufacturers to abandon the standards they now have and to take up others having different dimensions. Actual sizes can be determined accurately by means of the metric micrometer. Only the arithmetical value need be converted.

The United States of America can adopt metric standardization even though avoiding strange names. Old terms of yard, quart and pound can be preserved. English equivalents would do just as well for unfamiliar words in metrics. Why not say world yard for meter, world quart for litre and world pound for 500 grams? This is what they have done in Switzerland. As a result few people know that slight changes have been made in the units to make them metric equivalents. The German "pfund" of tobacco is 500 grams, the "fass" of beer is invoiced by its real contents in litres.

Metric Standardization would entail a negligible cost in changing weights and measures. Readings on expensive scales can be remarked at slight expense.

#### *Arguments Against the Adoption of the Metric System.*

Irrespective of any merits the metric system may have, the country, in case the system is made compulsory, will have to face:

(1) A long transition period; as a matter of fact, old units never disappear.

(2) The introduction of a dual system, because the habits of the people cannot be legislated away.

(3) A confusion between the two systems, becoming a most prolific source of error and expense.

(4) A cost appalling in its magnitude represented by the change involved in deciding on new standards, making new drawings, tools, fixtures, etc., which would seriously threaten during the transition period at least, our system of "interchangeable" parts.

(5) The re-calculation and establishment of new prices for every commodity raised and manufactured to conform with the new standards of length, weight and volume. (New catalogue.)

(6) The re-standardization of the products of industry and the re-writing of practically all our technical literature.

There are many important points raised by both sides, and there is need of careful consideration before formulating a decided opinion on the subject.

I. G.

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## ORIGINAL PAPERS

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### THE SIGNIFICANCE OF EDUCATION.

By WILLIAM H. CARPENTER, PH. D.

*Provost of Columbia University.*

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AN ADDRESS DELIVERED AT THE CENTENNIAL EXERCISES OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE, TUESDAY, JUNE 14, 1921.

In a search in the Columbia University Library recently for material bearing upon the early history of medical education in New York, we came across a pamphlet containing the address delivered at the Commencement, in 1819, of the College of Physicians and Surgeons, now of Columbia University, at that time under the temporary jurisdiction of the University of the State of New York, by Dr. Samuel Bard, President of the College. Dr. Bard, who was born in your good City of Philadelphia in 1742, had been Professor of the Practice of Medicine in old King's College before the Revolution; he had become in due time the chief practitioner of medicine in the City and Province of New York, and had the distinction of being the family physician of George Washington. The address, which is a truly remarkable one both as a statement and a prophecy, begins

with the following sentence: "A sound mind, in a sound body, constitutes the principal happiness and perfection of man; the means, therefore, by which such great and essential benefits are to be secured, have ever been the object of his solicitude, and most anxious inquiry." The statement, made a hundred years ago, was not new, nor was it in its main thought original. It is in reality but a paraphrase of what the Latin poet, Juvenal, said eighteen hundred years before him in that often quoted Latin phrase: "*Mens sana in corpore sano*," as constituting the ideal possession of a Roman youth.

The statement has appealed to me for the universality of its application. It would be quite impossible at the present time, or it will be impossible through the long years of history yet to come, to formulate the matter, either in its original epigrammatic form eighteen centuries ago, or in its paraphrase a century ago, as the essential fact in the existence of the individual, both for himself and for the part that he perforce must play in the social complex of his day and generation—for I take it as a self-evident truth that no man stands for himself alone in his out-goings and his in-comings, in his opinions and his prejudices, in his joys and his sorrows, in the manifold actions and reactions of human contact in the relationships of life, and that his mind and his body in their balance are a fundamental fact in the greater balance of the world of men beyond him.

If this fact then remains, as it seems to me to remain almost an eternal verity, that a "sound body" is an essential factor, and let us even say the essential factor of successful living, it is, after all, but a general statement that like such statements elsewhere is in need of what is sometimes called a definition of particulars to make it directly intelligible and applicable to any particular time. In point of fact, it has had at one time a meaning very different from what it has had at another, and while in a broad sense it has been always true, in a narrow sense of the actual accomplishment of result in the light of the understanding of a particular time, it has swayed backward and forward as the ideas of life and living have advanced or retreated on the long highway of human history. What I mean to say is that while the attainment of a sound mind in a sound body has been the educational ideal of the centuries—for it is a true definition of the purpose of education, as it has ever been—the means to attain it and the real results that it has been desired to attain have been as different as has been the whole varying course of human civilization. The serious ideals of one age have been at times the

ridicule of the next, and the little-regarded of one generation have been not seldom advanced by its successors at other times to positions of supreme importance as matters of belief, and it has even gone so far in history that the sins of one generation have been the virtues of the next.

The history of education, accordingly, as I desire to use the term, shows a constantly changing concept, even generation after generation, of the means of attainment and of the actual ultimate result to be attained to accord with the time and place, which shall constitute a man in the eyes of his generation as one with a sound mind in a sound body, or, as we may choose to phrase it, with an education that shall fit him to play his part on its recognized stage of action.

In a recent English essay on the need of educational reform, although in a wholly different connection, I find this matter stated much more clearly and concisely than I have done. "A new age," it says, "postulates a new education," and it is explained that "the traditions which have dominated hitherto must one by one be challenged to render account of themselves; that which is good in them must be conserved and assimilated, that which is effete must be scrapped and rejected." An education, I would add, that does not fit into the life of the time, not necessarily to subordinate itself supinely to it, but at least to recognize in its content and in the organization of its methods the inherent necessities of the day, is useless where it should be most useful as the very foundation of an advancing civilization.

If all these things are true, and I think in the main they are, the thought that readily occurs is what should be the nature and content of education at the present time, and what is its true significance in the life of the individual and in that of the community of which he, whether he will or not, is a constituent and participating part. For my present purposes I shall assume that a system of formal education that has any just claim to recognition as logically conceived and consistently carried out takes due account of a sound mind and a sound body as coincident factors of educational development. One of my colleagues at Columbia University a number of years ago wrote a book with the somewhat amazing title of "Why the Mind has a Body," and he went on to question the rather natural inference that mind and body are, in respect of action, on a footing of equality; in other words, that the temptation lies very near the surface to set up

the claim that every fact which shows the influence of body upon mind can be matched with a fact showing the influence of mind upon body. His ultimate conclusion, however, is that the dependence of mind upon body in the long run is only apparent, and that as an actual fact of existence the mind dominates the body, which is, after all, but the seat of organic life. Whichever is true—and such speculations run far afield—is beyond my present purpose. We must presuppose, I think, that it is an intention of education to secure by its processes the sound body that alone can support in its processes the sound mind, and that the school and the college, however imperfectly the results may actually be attained, are as alive today to the necessity of the correlation as were any of our forbears in the past. I hold no special brief for the particular form which the training of the body should take in the school or the college, since the matter must often be considered from the point of view of opportunity and environment, but that it should have a place, and a well-recognized place, as a fact and factor in any scheme of formal education is beyond argument. What I should have in mind, however, in school and college, is participant athletics—not the kind where the conscientious objectors sit comfortably on the bleachers and let the football team do all the rest. Even the professional school, where notably the work is intensive and the time is short, should find at least a modicum of space for athletic exercise, for a man who goes out to the practice of a profession with an ill-equipped body, however his mind may function, is handicapped from the start.

What, then, from the point of view of the mind—and of the soul—is the real significance of education, at the present time, not only to my generation which began with widely different ideas, and in some respects with very different ideals, from those of today, but to the generation that is now taking possession of the field as our successors in the activities of life; and what shall it be in its character and content to function, as needs must be, as a controlling impulse to lead not only the heads, but the hearts of men? "How can a man," says Carlyle, "without clear vision in his heart, first of all, have any clear vision in his head?" And long before him, it was pointed out that: "As a man thinketh in his heart so is he."

In making any definition of education, or in attempting any predication of its purpose and results, we must, of course, at the beginning fully recognize the fact that in the life of the professional man, the lawyer, the physician, or the pharmacist, there are two

elements involved, his education in his profession, on the one side, and his liberal education, on the other, or what we might properly call, at least from a certain standpoint, his special and his general education. My contention is that not for a moment is there any actual line of demarcation between the two. They are like two states of matter in flux that flow into each other until the whole is permeated by both and a new compound is formed that partakes of the nature of both elements, but yet in the end is neither. The lines of a professional education at the present time in its narrow sense of a special training for the practice of some one of its many phases are as a general thing well laid down, and the professional schools of the country of the best sort are more adequate in their equipment of men and methods and more reasonably sure of the competency of their professional product to understand and to cope with the problems of practice than ever before in our history. This is, however, but one part of the problem of education, for a man, and we must now be careful to say, in her share in the practice of the professions, a woman, who is trained in a profession alone, and no matter what that particular profession may be, is only half educated, for another half essentially important has been neglected. I should greatly doubt, however, when all is said, that any one of the good professional schools now walks consciously into such a slough of despond as to make its courses of instruction purely professional and nothing else, or at least does not base its professional training as a climax of formal education upon a basis of general culture. There are, nevertheless, from the very nature of the case, temptations to do so that must be borne in mind in the organization and conduct of every professional school, whether pharmacy, law, or medicine, or any other, that must be counteracted and discouraged. There is an insistent demand in an age that is distinctly materialistic for material results, and, in the characteristic hurry of the time, for their rapid production, and the young men and young women who are to go out into the world in the practice of a profession for themselves are confronted with a period of preparation, if care is not taken, too prolonged in age and expense to make it possible of accomplishment. These are real difficulties that confront every professional school in the proper carrying out of a scheme of education, and yet they must be rationally met or else that school has only half done its duty to those whom it has stamped with its approval at the end of its teaching. It may be true that the school in question has prepared its

graduates to make a living, which, to be sure, is one of the ends of existence and a very important end indeed, since a good deal depends upon it for the part you play or even whether you are alive or dead, but in the more perfect equipment for life, and that is what we are considering, the fact of merely being able to make a living, although it is essential to most of us, or the acquisition of wealth which is but its sublimation, is but one element and not the only one in the whole plan of existence, for the end of all real education is not to make a living, but to live!

And what about this other half in a scheme of education, concerning which we have been talking with such confidence as an element of human life? A wise man has said that "the aim of education is the knowledge not of facts, but of values," in the sense that "values are facts apprehended in their relation to each other, and to ourselves." The matter could not have been better stated, for it is certain that the mere accumulation of facts, whatsoever kind they may be, does not constitute an education, or knowledge of them an educated man. It plays no part to you or to me as a criterion of education, as it is sometimes made to appear, whether we know any part or all of a long list of what is, after all, but the uncorrelated material of education, and not the thing itself in its relationships and its proper adjustments into a body of knowledge which shall constitute a cultural whole. A man may have read through the whole *Encyclopedia Britannica* and have remembered its facts, and yet have failed wholly in securing an education in any real sense. Facts are no doubt the basis in essential ways of education. This is particularly true of the strictly professional part of education, where of necessity facts are the very bricks and mortar on which the superstructure of professional knowledge is built, but this presupposes no heterogeneous collection of the odds and ends of knowledge, but of the evaluation of the many facts with which a profession is necessarily concerned in their relation to each other and their fusion together into a connected product of immensely increased importance because of its cumulative force.

As to the true content of what is usually called a liberal education, although only too often it is illiberal in nature and amount, I again hold no specific brief. I have, however, a very definite opinion of what should constitute in the end that education which it is desirable to attain in order to give it its true significance in a scheme of living. Herbert Spencer's famous definition of biological life: "The

continuous adjustment of internal relations to external relations," is much more widely applicable than to the mere functional existence of the body, for it applies alike to the mind and soul of man, and it is the great and transcendent purpose of a true education to awaken the mind and soul and to bring them into harmony and adjustment with the conditions of life.

Education, then, is not mere instruction in the subjects of the school or college curriculum, whatever they may be, science, the classics, mathematics, literature, or history. These in proper balance are no doubt, in some measure or other, the legitimate means to an end, but they are that only in their proper function as factors in a combined result more important than any one of them. And just where the emphasis in subject instruction should lie I do not know, and the schoolmen themselves who are most directly concerned with this phase of formal education are by no means agreed as to what the ultimate worth to a trained mind this or that subject should be. The field is so broad that it is only possible to delimit and choose, but the choice need not necessarily be in every instance the same, and doubtless at the best, and whatever has been chosen, it will only partially accomplish its object. I am not like the Scotchman of ancient memory who was open to conviction, but would like to see the man who could convince him, or the man who liked any color so long as it was red. My own preference would be the classics, for I am old-fashioned, a science, because I believe in the new, English language and literature, a modicum of mathematics and a good deal of history, but I am open to conviction that that is not the only way to state the case, and that under the special circumstances at hand other subjects, in other proportions, might be selected as well.

The end, however, of a formal education is clear. It is so to train the mind and the soul that there shall be a foundation at least of the true appreciation of the values of the things of life. No one is, of course, educated in school or college, for education never ceases, now or at any time, in the normal existence of the individual. The student in the story that I have always considered somewhat apocryphal who rushed out of his college Commencement waiving his diploma in the air and shouting: "Thank God, I am educated!" was entirely too sanguine of the actual result that had been attained even by a college course. The story does not tell of his future history, but I greatly fear that it was one of disillusionment, for he surely must soon have realized that he was only at the beginning and not the end of an unceasing quest.



It is the province of education to point out the direction of the quest for knowledge and for the truth that ages ago it was said "shall make you free"—free to discriminate between the true and the false wherever they may appear, in the narrower ethics of the practice of a particular profession as well as in the broader affairs of civic and national life; free to discover and to understand the false claims of charlatanism in all phases of life and in whatsoever guise, or disguise, they may clothe themselves for the befoolment of the crowd; free to value at their real worth the passing fads and foibles of the moment that are but the froth borne along on the top of the wave that presently will recede and leave the wider surface unruffled as before; in other words, free to recognize that truth, and truth only, is eternal, and that all else sooner or later in God's good time disappears wholly from the sight of men, that it ultimately vanishes—an intangible shadow without substance or reality—back into the infinite space from which it momentarily has emerged and is forgotten!

There has been no greater need at any time of the educated man, and no time like the present time to keep these things in mind. I have always remembered a phrase used by President Butler in the address delivered at the Columbia Commencement of 1917. At that time, the Great War was still in its throes of death and destruction, but it was pointed out by the speaker that the world was more than a world at war, it was a world in ferment. What he meant was that the political and social conditions that always follow in the wake of war, and as a consequence of it, were like the chemical decomposition of an organic compound, and veritably were in a state of fermentation.

What was said then in the midst of the mighty struggle that was still going on is unfortunately as true today as upon the day on which it was spoken. The world is still in ferment. Old standards of conduct have been obscured, and sometimes forgotten. Old ideas of duty have apparently been laid aside. Old traditions of righteousness have been displaced in high places. New ideas of individualism and self-determination have swept away the multitude, and a new world, in many respects unlike the old, has taken its place. In spite, however, of all that is new and disturbing in conditions of the present which have followed as a natural consequence the destructive forces of the war, destructive to human conditions as well as to human life,

there are still, however, in the new world that has come about, the same fundamental standards of life and living. Whatever has been installed and whatever has been lost, there are still as deeply entrenched as ever the eternal verities that are the basis of human action. Truth may be obscured, but it is not destroyed; honesty may be in eclipse, but it is only hidden; personal conduct that controls the souls of men remains as it ever was, the fundamental fact of human and social existence. However much things seem to be in disorder and standards appear to be destroyed, at the bottom there is still the same basis of human action—action *as* an individual in living his own life for himself, action *in* the individual as he is a constituent and component part of the nation in which he lives. However the world may change, and however it has changed within your memory and mine, this is the fact that must remain still firmly fixed in our minds, that the old rules of conduct in the things of the mind and the soul are still always as they have been, and that these new conditions that confront us are often but the froth of the ferment, and the real, the fundamental facts of existence still remain, and will always remain the same. Life, as we have said, is infinitely more than organic existence. The life of all who are living today to enter into its fullest appreciation is not only the life of the body, but it is the life of the soul of man with its aspirations, its longings for results, its sacrifices and its achievements, and the men and women who go out into this new world from the professional schools to take their place in it should be equipped not only with a knowledge of the profession which they may have chosen for their own, but equipped also, as I think, with a knowledge of the value of the things of life to themselves as individuals, as I have tried to state it, and to the society in which they are to live and to act as its responsible members, and it should not be forgotten that these fundamental things that I have called to mind are the real conditions of a rational existence.

An individualism that thinks only of self and a determination that has only self for its object is, however, but half of the duty of man. A thought of self is necessary for self-preservation as a fundamental fact of existence, but the mind that stops there has only realized a part of the supreme significance of life, which not merely takes account of the individual to himself, but also in a broad and enlightened spirit makes him to himself a constituent and militant part of his environment and of his place in human society. In the background of it all is still, of course, the professional calling of the

individual. A great philosopher, Francis Bacon, three centuries back expressed this matter in terms that cannot be better stated today: "I hold every man a debtor to his profession, from the which, as men of course do seek to receive countenance and profit, so ought they of duty to endeavor themselves . . . to be a help and ornament thereunto." There can be, however, no thought to live for it alone, because, in the end, it is only one of the manifold parts of life.

A real education is more than a special equipment in any single direction of human energy, and its intention is to unfold to its highest potentiality the nature of man. The best definition that I have ever read of the true significance of such an education to the man who wears it as his crown of accomplishment is that contained in Huxley's "Essays," from which I copied it many years ago and have kept in sight as a precious possession. It is only a part of a longer statement of the position of man in the universe and his relation to it, but it bears directly on the present case, and this is what he says:

"That man, I think, has had a liberal education, who has been so trained in youth that his body is the ready servant of his will, and does with ease and pleasure all the work that as a mechanism it is capable of; whose intellect is a clear, cold logic engine, with all its parts of equal strength, and in smooth, working order: ready, like a steam engine, to be turned to any kind of work, and spin the gossamers as well as forge the anchors of the mind; whose mind is stored with a knowledge of great and fundamental truths of nature and of the laws of her operations; one who, no stunted ascetic, is full of life and fire, but whose passions are trained to come to heel by a vigorous will, the servant of a tender conscience; who has learned to love all beauty, whether of nature or of art, to hate all vileness, and to respect others as himself."

Such a man, it seems to me, has realized to the full the significance of education as I have wished it to appear in these somewhat scattered remarks this morning, fitted in his mind and soul to serve at least in partial fulfillment of the purpose of what long ago was called "the great appetites of honor."

## ECONOMY OF TIME IN PERCOLATION.

By DR. ROBERT A. HATCHER.

*(With Technical Assistance of Miss Anna Lichtman.)*

The Pharmacopœia directs that when an official tincture is to be made by percolation the moistened drug shall be allowed to stand during a period of six hours before it is packed in the percolator, and that when the liquid begins to drop from the lower orifice of the percolator, the drug shall be allowed to macerate during a period of twenty-four hours before the percolation is allowed to proceed.

It is desirable that the moistened drug shall not stand for a longer period than is necessary for the menstruum to penetrate thoroughly into the cells before being packed in the percolator, and that maceration shall not then continue unless it is necessary for the extraction of the active principles, otherwise time is wasted and alcohol is lost by evaporation. Furthermore, the longer the time consumed in making tinctures the greater is the investment in apparatus and floor space required for a given number of operations when these are sufficiently numerous to demand that several shall be conducted simultaneously. This is a matter of importance to large manufacturing pharmaceutical establishments.

It is probable that the period of six hours during which the moistened powder stands before being packed in the percolator suffices for the penetration of the menstruum into the cells of the drug; if this is not the case the fact should be determined by experiment, and a greater amount of menstruum should be used for moistening the powder, or it should be allowed to stand for a longer period of time before it is packed in the percolator.

Nux vomica, strophanthus, and aconite powders in portions of 100 grammes each were used in the experiments designed to show whether it is necessary to macerate the powder after the liquid begins to drop from the percolator in the preparation of the official tinctures of these drugs.

The percolation of the nux vomica was allowed to proceed (without this period of maceration) until 1000 cc. of percolate were obtained, and the marc was then percolated with a portion of the same menstruum until 500 cc. of weak percolate were obtained. The activity of the tincture and that of the weak percolate were then de-

terminated by means of the biologic test on frogs. The protocol of the experiment (in brief) which follows shows the tincture represented the drug almost completely, and that the activity of the weak percolate was equal to only about 1 per cent. of that of the tincture.

PROTOCOL (IN BRIEF).

One hundred grammes of nux vomica in No. 60 powder were moistened with menstruum consisting of a mixture of three volumes of alcohol and one volume of water; the moistened drug was transferred to a percolator and allowed to stand three hours (instead of six hours, as directed by the Pharmacopœia), after which it was packed firmly, menstruum was added and percolation was allowed to proceed at once until a total of 1000 cc. of percolate was obtained in a period of forty-four hours. Percolation of the marc was continued until 500 cc. of weak percolate were obtained.

The activity of the tincture and that of the weak percolate were estimated by determining the amounts required to kill a given weight of frogs after injection into the lymph sac. The tests showed that 1000 cc. of the tincture would suffice to kill about 400 kilos of frogs, and that the weak percolate would suffice to kill about 2.5 kilos. This shows that the activity of the weak percolate was less than 1 per cent. of that of the tincture.<sup>1</sup>

The results of this experiment show that it is not necessary to macerate nux vomica after the liquid begins to drop from the percolator in order to insure the practically complete exhaustion of the drug when making the official tincture, provided the moistened powder has been allowed to stand for a period of several hours before being packed in the percolator.

It seemed desirable to compare the activity of the first portion of percolate and that of the finished tincture made in the manner just described with the activity of the weak percolate, hence the procedure was modified in the preparation of the tinctures of strophanthus and aconite. A portion of 250 cc. of the first percolate of each of these was put aside, and percolation was allowed to proceed

<sup>1</sup>Frogs usually require about 5.5 mg. of strychnin sulphate per kg. of weight to cause death when the poison is injected into the lymph sac in solution containing 1 part of the poison to 1000 parts of normal salt solution. Some lots of frogs show closely concordant results, whereas others show greater individual differences. The results in this experiment were not exactly uniform, but the agreement was sufficiently close for the purposes of this investigation.

until 750 cc. of additional percolate were obtained in each case, after which the marc was percolated with a fresh portion of the official menstruum, and this weak percolate was put aside. The activity of each of the several portions of percolate was then estimated by means of the biologic test on cats. The protocol (in brief) of an experiment with each of these two drugs follows.

*Strophanthus*.—One hundred grammes of strophanthus in No. 60 powder were packed in a percolator, this was percolated with purified petroleum benzin to remove fat, the defatted powder (weighing 74 grammes), was then moistened with alcohol and allowed to stand two hours (instead of six hours), after which it was packed firmly in a conical percolator, alcohol was added and percolation was allowed to proceed at once. The first portion of 250 cc. of percolate was obtained in a period of about twenty-one hours, and the second portion of 750 cc. in the succeeding period of twenty-nine hours. Percolation of the marc was continued until 250 cc. of weak percolate were obtained.

The activity of the several portions was estimated by the method described by Hatcher and Brody. (AM. J. PHARM., 1910, Vol. 82, p. 360) The activity of the first portion of 250 cc. was equal to about 17,780 cat units (this amount would suffice to kill 17,780 kilos of cats with intravenous injection); the activity of the second portion of 750 cc. was about equal to that of the first portion of 250 cc. (the total activity of the mixed first and second portions being about 35,000 cat units); the activity of the weak percolate was equal to about 926 cat units.

These results indicate that the first portion of only 250 cc. contained about half of the total of the active principles of the seed, that the second portion of 750 cc. contained rather less than half, and that the 250 cc. of weak percolate contained about 2.5 per cent. of the total active principles.

*Aconite*.—One hundred grammes of powdered aconite<sup>2</sup> were moistened with menstruum consisting of a mixture of three volumes of water and seven volumes of alcohol, and allowed to stand during a period of two hours, after which it was packed in a percolator,

<sup>2</sup> The powder used in this experiment was obtained from a reputable firm and was labeled No. 60 powder, but was evidently about No. 80 powder.

menstruum was added and after thirty-two minutes the liquid began to drop from the lower orifice of the percolator, but percolation proceeded so slowly that suction was applied, and 250 cc. of percolate were obtained in fifteen hours—the last 64 cc. of this in twenty-one minutes—and this portion was set aside. Percolation was continued and the second portion, measuring 750 cc. was obtained in the next period of about seventy-two hours. Menstruum was added to the marc and 250 cc. of weak percolate were obtained.

The activity of the several portions of the percolate were estimated by determining the amounts required by intravenous injection to kill a given weight of cats. The test showed that the first portion of 250 cc. of percolate would suffice to kill about 2000 kilos of cats, that the second portion of 750 cc. would suffice to kill about 300 kilos, and that the weak percolate would suffice to kill only about 20 kilos, or less than 1 per cent. of the total of the first and second portions.

#### DISCUSSION.

The results obtained with tincture of *nux vomica* and tincture of *aconite* speak for themselves and do not require detailed discussion, but it is interesting to observe that the first portion of 250 cc. of percolate obtained from the *aconite* in a period of fifteen hours—without previous maceration, except for the two hours during which the moistened drug was allowed to stand before being packed—was about eighteen times as active as an equal volume of the last portion of 750 cc. which was obtained by percolation during a period of seventy-two hours.

One may be disposed to argue that the failure to exhaust the powdered *strophanthus* completely affords evidence for the need of the preliminary maceration directed by the *Pharmacopœia*. Against this is the fact that a given volume of the first portion of the percolate was about three times as active as an equal volume of the second portion. The explanation of the failure to exhaust the drug completely in this case is to be sought in the physical properties of the drug and its active principle.<sup>3</sup>

The cells of vegetable drugs afford extensive surface areas which, by virtue of their capacity for adsorption, retain traces of many active principles with extraordinary tenacity, and in such cases the exhaustion of the drug is dependent upon the character of the solvent and the volume employed to a much greater degree than

upon the duration of the period of contact of the menstruum with the drug. Evidence in support of this is afforded by the results of an experiment carried out in this laboratory some years ago. One thousand grammes of powdered digitalis were percolated with ten liters of the menstruum directed by the U. S. Ph., VIII, during a period of about three months with periods of maceration. The last portion of about 3000 cc. of percolate represented the activity of about two grammes of the powder.

It is difficult to understand what advantage can result from the maceration of the drug for a period of twenty-four hours after the menstruum begins to drop from the percolator if the menstruum had penetrated thoroughly into the cells of the drug previous to its being packed tightly into the percolator. The higher the percentage of the active principles present in the drug the more rapidly will they pass into solution in the menstruum up to the point of saturation, and conversely, the lower the percentage present the more slowly will they pass into solution.

From this it follows that if maceration is required at any time (after the preliminary period before the drug is packed) it will be toward the end of the percolation when the powder is nearly exhausted. If percolation is not too rapid the drug will be practically exhausted by a suitable menstruum without this period of maceration.

#### SUMMARY.

Tinctures of aconite, nux vomica and strophanthus were prepared without macerating the drugs after the liquid began to drop from the percolator.

The tinctures prepared in this way represent the activity of the drug almost completely.

The first portion of the percolate is much more active than the last portion; the first portion of the percolate of aconite was at least eighteen times as active as the last portion.

<sup>3</sup> There is some evidence that alcohol is not the best menstruum for making tincture of strophanthus. A tincture of strophanthus was prepared with a menstruum of 65 per cent. alcohol in this laboratory several years ago, at which time the several fractions of the percolate were tested for their activity. It was found that the first portion of percolate, representing one-tenth of the volume of the finished tincture, contained 65 per cent. of the active principles, and the second portion of equal volume contained more than 75 per cent. of the balance, the remainder of the percolate containing about 10 per cent.



Adsorption by the cells of the drug plays a variable role in the exhaustion of drugs, certain active principles being retained in the marc with great tenacity. The effectiveness with which active principles are retained by reason of adsorption depends more upon the solvent used than upon the length of time during which the menstruum is in contact with the drug beyond that required for ordinary slow percolation.

Maceration of the drug for a period of twenty-four hours after the liquid begins to drop from the percolator and before percolation is allowed to proceed is unnecessary, and results in loss of time, in the manufacture of tinctures.

Biologic tests were made to determine the activity of the several fractions of percolate.

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## THE STATUS OF PREREQUISITE LAWS AND PHARMACEUTICAL LICENSURE.\*

By J. W. ENGLAND.

The enactment of the prerequisite law of the State of New York effective as of January 1, 1905, and of the State of Pennsylvania effective as of January 1, 1906, affecting the two most populous States of the Union, marks an epoch in the history of pharmaceutical education and legislation in this country. The surprising feature of this legislation, however, is that the importance of systematized pharmaceutical education as a prerequisite for examination to practice was not legally recognized for nearly one hundred years after the establishment of pharmaceutical education in this country by the Philadelphia College of Pharmacy in February 23, 1821.

H. C. Christensen, Secretary of the National Association of Boards of Pharmacy, writes me (May 9, 1921) as follows:

"After the enactment of the prerequisite laws in New York and Pennsylvania, there followed a long period of inactivity along this line, or possibly more correctly a period of propaganda without apparent results until 1915, when the North Dakota and State of Washington Boards of Pharmacy adopted prerequisite requirements

\*Read at annual meeting of Pennsylvania Pharmaceutical Association, June, 1921.

by rulings of the Boards. Illinois and Ohio followed with prerequisite laws becoming effective July 1, 1917.

"The seventeen States, including those mentioned above, in which prerequisite legislation has been enacted up to January 1st of this year, are as follows:

New York	Kentucky	Rhode Island
Pennsylvania	Maryland	South Carolina
Illinois	Minnesota	Virginia
Ohio	New Jersey	Washington
Indiana	North Dakota	Mississippi
Iowa	Oklahoma	

"Oregon has a requirement for one year college work, effective 1921, and graduation effective 1922.

"The five States which have reported that prerequisite legislation has been passed so far this year are West Virginia, by ruling of the Board, North Carolina, Kansas, Nebraska and Texas. Prerequisite legislation is pending in several other States where legislatures are still in session. Alabama, Michigan, Georgia, and a number of other States where conditions were not favorable this year will seek prerequisite legislation in 1923."

By these data, it will be seen that less than one-half of the States of the Union have prerequisite laws, and earnest and determined steps should be taken by the pharmacists of every State not having a prerequisite law to secure the enactment of such legislation, not only for the good of American Pharmacy, but what is more important, the better service of the American people.

Almost as important as prerequisite legislation, is the matter of reciprocity in pharmaceutical licensure and on this question Mr. Christensen writes me:

"Reciprocity in pharmaceutical licensure is in force between forty-three States and the District of Columbia—the list given at the bottom of this page.<sup>1</sup>

"The procedure for reciprocity is by agreement between the State Boards of Pharmacy of the various States using this office as

<sup>1</sup> Active member States between which reciprocity is in force: Alabama, Arizona, Arkansas, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Mexico, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin.

a clearing house. The applicant for reciprocity secures the official reciprocal application blank from this office on payment of the required fee of \$15 (which fee goes for the up-keep of the National Association of Boards of Pharmacy and the bringing-about of uniformity in examination methods, etc., in the various States). Certification as to registration and grades must be made on this blank by the Secretary of the State Board of Pharmacy in the State where he is registered by examination. The application then goes to the Secretary of the State where registration is desired, with the required amount of State registration fee.

"By agreement between the various Boards of Pharmacy certain minimum requirements were adopted at the time of the organization of the National Association of Boards of Pharmacy with reference to standards, etc., which a State Board of Pharmacy must come up to in order to have their licentiate recognized in other States. Since these minimum requirements were adopted, the Association has endeavored to consistently advance the standards in the various States from time to time, and an applicant for reciprocity must meet these higher standards, providing he was registered since they went into effect. This plan of reciprocity is working out very satisfactorily, both with reference to accommodating those who wish to go from one State to another, and also tends to raise the standards of all States, since those States lagging behind lose the benefits of reciprocity for their recent licentiates."

In this connection, Lucius L. Walton, Secretary of the Pennsylvania State Board of Pharmacy, writes me (May 2, 1921) as follows:

"In the list of active member States between which reciprocity is in force, the reciprocity exists between them in so far as the laws of the respective States will permit. In addition to this list is New York as an associate member, approving and supporting the organization, but holding aloof from participating in the reciprocal methods of the Association.

"The affiliated active list gives evidence of the general approval of the organization by the Boards of Pharmacy of nearly all of the States. The attendance upon the annual meetings of the National Association of the Boards of Pharmacy gives evidence of the interest and desire upon the part of at least 60 per cent. of the boards to perfect the organization and bring about uniform requirements and methods for determining the same.

"At the meeting of the Second District of the Boards held in Atlantic City last November, the New York delegation agreed to propose that reciprocity be adopted by the Board of Regents of the State of New York, based upon the qualifications of the individual

applicants.<sup>2</sup> This is really what we do in Pennsylvania. Originally the prerequisite provision of State laws were so drawn that there could be no reciprocity unless the participating States had the same legal requirements for registration.

"The National Association of Boards of Pharmacy represents the State Boards of forty-three States and the District of Columbia; it does not represent California, New Jersey, Rhode Island and Wyoming, while New York has only associate membership.

"Our national organization cannot compel any State Board to make a reciprocal registration if it does not want to make it. It represents the consensus of opinions of its constituent members on all questions relating to requirements and examination methods through its constitution and by-laws, which the members are expected to co-operate in making effective, except when the law of some State prevents."

The National Association of Boards of Pharmacy was organized in Kansas City, Missouri, in September, 1904, in accordance with a resolution passed by the Mackinac meeting of the American Pharmaceutical Association in 1903.

By these facts, it will be seen that the National Association of Boards of Pharmacy has contributed more probably to the advancement of the legal standards of pharmacy than any other single agency. In later years it has had the co-operation of the American Conference of Pharmaceutical Faculties (organized in 1900), which has done much to aid the organization in its work for the legal betterment of the practice of pharmacy.

Pharmaceutical education and legislation should go hand in hand, to the end that the interests of pharmaceutical education may be promoted, pharmaceutical legislation made more effective, and public service improved.

<sup>2</sup> Warren L. Bradt, Secretary of the New York State Board of Pharmacy, writes me as follows: "Replying to your letter of May 25, I am advising you that no action has been taken by this Board recommending to the Board of Regents reciprocity of licenses with any other State Board."—J. W. E.

## BLOOD COAGULANTS.\*

By LOUIS GERSHNFELD, PH. M., B. SC.,

*Professor of Bacteriology and Hygiene, Philadelphia College of  
Pharmacy and Science.*

Blood Coagulants may be divided into two classes: (a) Non-specific, and (b) Specific types. Under the first class are included the metallic salts and others which act by directly precipitating proteins. They are more frequently known as Hemostatics. One can readily see that the latter can only be employed in accessible hemorrhages. It is impossible to employ them in inaccessible hemorrhages as death would result when such substance would be injected into the blood stream.

The so-called Specific Blood Coagulants are of recent origin, and their introduction are as a result of a more thorough understanding of the theory of the Coagulation of Blood, which at one time was thought to be nothing more than a reaction between a so-called Fibrin Ferment on the protein material in blood (Fibrinogen) with the production of fibrin and the typical blood clot.

The writer thinks that pharmacists should know more about these products, as they may have occasion to dispense some of them.

An intelligent understanding at such occasion may result in a complete satisfaction to all concerned.

The first of these products employed extensively was Normal Blood Serum.

NORMAL SERUM from humans, but usually from different animals (especially the horse), though not a specific immunity product has been employed in the treatment of hemorrhage to increase the coagulability of the blood.

The serum is usually obtained from a normal animal under sterile precautions. The product is passed through a Berkefeld filter, sterility and toxicity tests are performed, and it is then marketed in sterile containers.

The principle of its action when employed (as it may be locally or in doses of from 10 to 30 cc. subcutaneously, intramuscularly or in critical cases intravenously) is as follows:

\* Read before a meeting of the Penna. Pharm. Assoc., June, 1921.

The clotting of blood is not as simple an operation as it ordinarily seems. A substance exists in the blood stream, which is known as prothrombin. The latter reacts with the calcium salts to form an enzyme known as THROMBIN OR THE SO-CALLED FIBRIN FERMENT. During bleeding, the fibrin ferment (which does not seem to be a ferment at all) acts at once on the fibrinogen (a protein material normally present in blood plasma) to form an insoluble substance known as FIBRIN. This forms in shreds within which are held the elements of the blood, this mass in turn giving rise to what is commonly termed a blood clot.

If this theory would be accepted as it stands, the question may arise why blood does not clot spontaneously in the tissues.

Howell (*American Jour. Phys.*, 29, 187, 1911) has advanced a modification of this theory, which is as fully and firmly founded as any theory as yet brought forth. He claims that in addition to fibrinogen, prothrombin and calcium salts, normal blood contains another constant element which he calls antithrombin. The latter possesses the property of preventing the changing of prothrombin into thrombin in the circulating blood. During bleeding, however, the broken down blood cells (especially blood platelets) or tissue cells seem to furnish a substance (called THROMBO PLASTIC SUBSTANCE OR THROMBOPLASTIN), which unites with, neutralizes or inactivates the Antithrombin thus liberating the prothrombin. The latter in the presence of the calcium salts forms thrombin which reacts with fibrinogen, producing the blood clot.

In many cases of all types of hemorrhage, an individual may bleed to death due to a defective power of coagulation. Lack of coagulating properties may be due to many reasons, the important one being, a deficiency in prothrombin (due to its absence or on account of its complete neutralization by antithrombin). The principle of the normal serum treatment consists in supplying the active ferment (present in the latter) to such patients, lacking the active coagulating principle, or as thought by some, its value may be due to the presence of thromboplastic substance.

Horse serum loses its efficiency upon standing. It was also found to be harmful at times due to pronounced anaphylatic reactions, which may result in severe shock and even terminate fatally.

Investigators were therefore let to isolate the clotting principle or produce a substance which would assist in coagulation.

As soon as Howell put forth his theory, a new thought was ad-

vanced for the lack of normal coagulating properties. It was suggested that an insufficient production of Thromboplastic substances may also retard coagulation, inasmuch as only a portion of the anti-thrombin would only be acted upon. This would still leave some of the prothrombin intact, and only the released prothrombin would be capable of exerting the coagulating effect, which would undoubtedly be diminished.

Howell upon further investigation showed that this "thromboplastic substance" or "thromboplastin" contains a phosphorized fat known as "Kephalin," or "Cephalin," and that the latter was the actual substance of the Thromboplastin which influenced coagulation.

Kephalin, a fat containing phosphorous (called a phosphorized fat) is also an important constituent in nervous tissue (especially brain and spinal cord) and present in larger quantities here than in any other tissue.

Preparations containing Kephalin, the underlying principle of Thromboplastin were soon prepared from ether extractions of the brain and spinal cords of mammals (sheep, of cattle, etc.). These products alone, or admixed with normal serum or extracts from normal serum or dried blood and blood platelets are marketed as efficient blood coagulants under various names as:

Brain Lipoid, Solution of Brain Extract, Thromboplastin, Hemoplastin, Coagulen, and Coagulose.

It is at times impossible to determine just what element is lacking which may result in an increase in the coagulation time of blood in an individual. Such a defect must be remedied if the patient is to undergo surgical operation, etc. In some instances it may be due to a deficiency of calcium. This can be easily remedied by administering calcium salts.

At times there may be a deficiency of prothrombin while the Kephalin products are useful in supplying thromboplastin which may be lacking in other instances.

These specific Blood Coagulants are employed hypodermatically, intravenously, etc., for the treatment of inaccessible hemorrhages, and by local application in accessible hemorrhages. They have been employed with considerable success in many cases, but as yet as far from a true specific in the treatment of all causes of hemorrhages, accessible or inaccessible.

Their use is not as extensive as might be due to the fact that

there has not been introduced as yet an efficient method for standardizing them.

These preparations are standardized by different methods, in many instances, each manufacturer using a supposedly pet method supplied by their own laboratories. It would be advisable to adopt a uniform method for standardizing these products which should be approved by the Hygienic Laboratory and recognized in the next revision of the Pharmacopœia (as are other biological assays). The U. S. P. might at the same time include a method or procedure for making an efficient specific blood coagulant.

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## CONSTRUCTIVE PUBLIC SERVICE IN PHARMACY.

By CHARLES H. LAWALL, PH.M.

*Address Delivered at the Centennial Celebration, Tuesday,  
June 14, 1921.*

During the several thousand years through which the profession of pharmacy may be historically traced, it has undergone many interesting changes and vicissitudes. Its evolution has been irregular and in some respects disappointing. The reason for this is found in its lack of uniformity. It has always been heterogeneous, and its heterogeneity has been variable.

The physician-pharmacist was successively replaced by the alchemist-pharmacist, the grocer-pharmacist, the chemist-pharmacist, and later by the merchant-pharmacist. Through all these metamorphoses there has, however, remained a distinctiveness of service which has been obscured at times, but which in its fundamentals has retained one important phase of public contact and service—the preparation and sale of medicines.

From the most primitive beginnings, in which mysticism and credulity prevailed, and in which empiricism held full sway, down to the present time, when a highly specialized technical and scientific training is required by the State for the protection of the public which pharmacy serves, the dominating purpose has been to assemble, identify, select, preserve, prepare and standardize remedial substances, which in the hands of the careless or unskilled might prove detrimental instead of beneficial.

The history of this famous art is a fascinating chapter of human



progress and endeavor. It has its roots in the misty ages of the Orient and among the races of mankind contributing to its improvement were the Babylonians, Egyptians, Greeks, Romans and Arabians.

Differing in detail as to its practical application, the landmarks are shared by its practitioners in all lands and under various designations. Every civilized country has its pharmacopœia, the *vade mecum* of the pharmacist, and largely the result of his labors and researches. The United States Pharmacopœia, now undergoing its tenth decennial revision, is the second oldest of these national authorities (the *Codex Medicamentarius* of France being the oldest), and in its technical details is a monument to American Pharmacy, which has largely been entrusted with its preparation.

Pharmaceutical education was inaugurated in America by the apothecaries of the City of Brotherly Love when they founded the Philadelphia College of Pharmacy, one hundred years ago. Since that time it has undergone many improvements and changes, as have all other fields of education, but its progress has been retarded largely because of the lack of supporting legislation in many of our States. After many years of waiting we may say with confidence that pharmacy is now on the verge of a great advance in this respect and that in the next ten years more progress will be made than has taken place in the last half century.

There has been no lack of appreciation of what has been needed, but there have been certain forces to combat and prejudices to overcome and much preparatory work to be done. In this connection, credit must be given to the constructive efforts of the American Conference of Pharmaceutical Faculties, composed of representatives of over forty leading colleges of pharmacy of the United States, which has labored unceasingly for twenty years for the adoption of higher standards and the elimination of schools operated for profit alone and not for service to the community.

There has been no failure on the part of the colleges, meanwhile, to educate the students to properly qualify under the State registration laws. The shortcomings have been in not recognizing the necessity of a broader cultural education to accompany the scientific and technical training. The pharmacist of a decade hence will be on a par as regards his preliminary education and cultural training, with the members of other learned professions and insensibly and auto-

matically many of the inconsistencies and evils of the present practice will disappear for all time.

More and more pharmacists each year are fitting themselves for wider public service by taking special courses in bacteriology, clinical chemistry, technical analysis, and sanitation, and are becoming valuable aids in public health work and analysts and experts in their respective communities. The stimulation in this direction has been especially noticeable since the close of the war, for it was during that period that many came to realize the value of scientific training and the opportunities which are open to one who qualifies along such cognate lines of study.

The interdependence of pharmacy and medicine was never more in evidence than at present, for with the introduction of biological preparations, including sera and vaccines, and the discovery of new methods of preparing and standardizing long used drugs, the physician is more than ever compelled to rely upon pharmacy for distinctive and important scientific assistance. Pharmacy and medicine have common battles to fight in combating the manufacture and sale of worthless nostrums, and in educating the public along correct scientific lines of hygiene and health conservation.

They are co-sharers, under the law, of certain compelling responsibilities which have to do with the control, regulation and distribution of drugs which are known to be habit-forming, and of alcoholic preparations. It is a gratifying fact that the large majority of the members of both professions are true to their trust and worthy of the confidence reposed in them.

The opportunities for advancement, therefore, on the part of a great institution like the Philadelphia College of Pharmacy and Science, which serves pharmacy primarily and medicine indirectly, are convincing in their evident necessity. Among the more important phases of this advanced work are the following:

1. *The conducting of popular scientific lecture courses*, in which the public shall not only be given correct concepts of the scientific facts of importance in connection with pharmacy and the allied sciences, but the combating of error and superstition, which will also be an important part of this constructive work.

2. *The development of research service to the medical profession.* Medicine is already indebted to pharmacy for much con-

structive help in the scientific preparation of effective remedial agents and their standardization, thus allowing uniform results to be obtained under specific conditions. None but physicians and pharmacists realize how much of this work yet remains to be done. The lack of constructive, co-operative work in this direction has been productive of much of the therapeutic nihilism of the recent past.

3. *The institution of research departments which shall aid the manufacturing interests allied to pharmacy.* While a number of the larger pharmaceutical manufacturing establishments have well-equipped and efficient research departments, there are hundreds now without such service. It is to supply this evident need and to supplement existing work that such departments are to be instituted and maintained.

4. *The founding of laboratories for the express purpose of serving the City and State* in an impartial solution of problems such as the quality of supplies, the wholesomeness and purity of foods, the purity of drugs and chemicals, and other scientific questions affecting the public welfare.

These proposed benefits are self-evident. It is of tremendous value to any community to have available a corps of scientific workers capable of helping to solve routine problems. Such an organization in times of stress and emergency, as of war or epidemic, might be invaluable as an insurance against calamity due to lack of scientific preparation.

5. *The development of pure scientific research.* The lessons taught during the World War, as regards the value of pure science, were tremendously convincing. Pure science is only relative. The pure science of today becomes the applied science of tomorrow, and the nation that falls behind in pure scientific research will surely perish, if there ever comes another world war, which God forbid.

6. *The development of a public museum of drug and chemical products and pharmaceutical and chemical manufactures,* which will be distinctive for its breadth and modernity, as well as unique in its exhibits of historic value, for the College collections are especially rich in illustrative material of this kind, which now lack space for exhibition. With our present collection as a nucleus, adequately housed and under efficient full-time curatorship, such a museum could be

made the Mecca for scientific workers in our particular field, as some of our exhibits are very complete and are now frequently consulted by those searching for type specimens, or those illustrative of a certain period.

7. *The creation of a botanical garden particularly devoted to plants of medicinal and economic importance*, in order to stimulate and develop our national resources along new lines and to supply material for medical, chemical and pharmaceutical research.

8. *The proper housing of our present library of more than twenty thousand volumes of scientific works*, frequently consulted by scientists from afar on account of the rarity of some of its volumes.

In partial furtherance of these laudable ambitions there has been planned a series of courses leading to the degree of Bachelor of Science in Pharmacy, in Chemistry, in Bacteriology and in Pharmacognosy. These courses have been outlined and curricula prepared under the approval of the Pennsylvania Department of Education, so that there is a proper balance of cultural and technical subjects, making them equal in this respect to the Bachelor courses of any college of arts and sciences.

These courses will be inaugurated at the beginning of the next scholastic year and have been especially planned so as to cover the subjects required for entrance to the study of medicine. It is believed that they will be particularly acceptable to medical colleges as pre-medical courses, for what better preparation for medicine could there be than a four-year course based upon one of these scientific branches?

A course of fifteen popular lectures upon scientific subjects, to be given by members of the Faculty of the College, has also been planned for the next College year. These include a great variety of timely topics and will doubtless be well attended and much appreciated.

With such a programme of disinterested and constructive public service, we feel that the Philadelphia College of Pharmacy and Science is entitled to the support and approval of the profession which it represents and the community which it serves, and that the close of its second century will find it in the front rank of institutions venerated for their history and acclaimed for their achievements and the excellence of their work.

When we pause to survey the new vista and see the wider horizon, we feel that the measure of our opportunities is well expressed by Rosetti:

"Nay, come up hither, from this wave-washed mound unto the furthest flood brim look with me. Then reach on with thy thought 'till it be drowned; miles and miles further though the last line be, and though thy soul sail leagues and leagues beyond, still leagues beyond those leagues there is more sea."

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## ABSTRACTED AND REPRINTED ARTICLES

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### SAL CATHARTICUM AMARUM.\*

BY WILLIAM KIRKEY, M. SC.

EPSOM SALT.

There is, perhaps, no more characteristically English medicine than what was known in the eighteenth century as *sal anglicanum* or *sal catharticum anglicanum*, or, in the vernacular, Epsom salts. A quite rare pamphlet gave the first account of the production and properties of this drug. It was written by a physician whose name is best remembered by his work in the field of vegetable and animal anatomy. It is: "*Tractatus de Salis cathartici amari in Aquis Ebeshamensibus et hujusmodi aliis contenti Natura et Usu. Authore, Nehemia Grew, M.D. Utriusque Regiæ Societatis Socio, Londini, 1695.*" It is a small duodecimo volume of 96 pages. In Ince's "A Century of Old Books," A. F. Haselden describes a translation of this which was made by Dr. Joseph Bridges, "with animad-versions on a late corrupt Translation by Francis Moulton, Chymist, London." I don't happen to possess Bridges' translation, but I do possess, in addition to Grew's original, the translation by the said Francis Moulton, although it does not bear his name. It is more interesting as a specimen of smart advertising than for any other reason. The title reads: "*A Treatise of the Nature and Use of the Bitter Purging Salt contain'd in Epsom and such other Waters, by Nehemiah Grew, M. D., Fellow of the College of Physicians and of the Royal Society, London. Printed in the year 1697.*"

\*Reprinted from the *Pharm. Journ. and Pharm.*, May, 1921.

The translator's "To the Reader" is quite convincing with its air of honest transparency. "The Reason of my publishing this Book in English is, the general Use I observe to be made of the Bitter Purging Salt in this town and elsewhere, by all sorts of Persons, and that promiscuously, in all cases, as People's Fancies or Humours prompt 'em, without any Advice beyond Publick Fame, or the good Woman last visited.

"The Sellers of this Salt are likewise such as use to dispose of other Catholick or Universal Medicines, who neither know how to direct the Buyer, nor care what becomes of the Taker, so as they attain their End, their part of their Profit. There is indeed this difference: That other Medicines that have grown Popular were always usher'd out with printed Directions, or Certificates of its Virtues and numberless cures, as Daffy's Elixir, Spirit of Scurvy-grass, Atkins' Oil for the Gout, etc. Nay, the very Disciples of Ponteus afford for publick Benefit a printed Encomium for a Voucher to the Twelve-Penny Packet. This I thought sufficient to Vindicate my Translation of Dr. Grew's Nature and Use of the Bitter Purging Salt, which I intend to give to those who buy any quantities of the Salt. And I'd have the Reader take notice, That this is no Quack-Bill, no boasting Rhodomontado of any Ignorant Pretender, no guilded Bush to set off bad Wine, but the Observations of an Ingenious Physician, Fellow of both Societies, and published by him in Latin, for the information of the Practicers of Physick, and for no private Interest or Profit. But I can scarce believe the Doctor ever foresaw the Consequence of his Commendations wou'd be the pushing every Body upon the Use of it Hand over Head; therefore I doubt not his Pardon for my Translating it without his Knowledge, my Design being not to discover the Secret Method of its Preparation, but to prevent by these Directions the Mischiefs he tells us may ensue the Abuse of so good a Medicine. Farewell."

The first part of the pamphlet deals with the nature of the salt, and the second part with the use of it. Grew tells us that the Epsom spring was discovered "in or about the year 1620." It seems to have been found a little earlier—namely, in 1618, at least, Thomas Fuller says so—by a farmer called Henry Wicker, who noticed that his cattle refused to drink the water on the land, notwithstanding that it was a dry season, and who on tasting it himself found that it was bitter. For about ten years the water was used by the country people as an external remedy for ulcers, but by the middle of the seventeenth century the Epsom spring had acquired a considerable reputation as a medicinal water for internal use. Grew says that

"the Lord Dudley North, Father to Francis the late Lord-Keeper, labouring under a Melancholy Disposition for which he had formerly Drank the Spaw-Waters in Germany, was resolved to try the Virtue of these Epsom Waters, flattering himself (I suppose) that he had found Chalybeate-Waters at his own Door. However, tho' they answered not his desire and expectation as to their Nature, yet he did not repent of his Experiment, but from that time drank these Purging Waters, as a Medicine sent from Heaven, with abundance of success. Many others, encouraged by his example, try'd the operation of these Waters; and amongst the first, Maria de Medicis, Mother to the Wife of King Charles I., the Right Honourable George Lord Goring, Earl of Norwich, and many other Persons of Quality. These and all others, who drank the Epsom-Waters, came not for pleasure but Health, and therefore always consulted their own, or some Neighbouring Physician, for the Rules they were to observe. In a little while Physicians came of their own accord to these Waters, by whose authority they acquir'd so great a Reputation that 2000 Persons have been there in one Day, to drink or divert themselves.

"About 30 years since, many of the Inhabitants of London, whose Business or Poverty obstructed their going to Epsom, had the Waters sent to them."

Charles II and his Court went to Epsom "to divert" themselves, and later Prince George of Denmark, the Consort of Queen Anne, drove there from Windsor to drink the waters. Pepys, in his diary, has several references to his visits to Epsom. In 1664, we find him recording that "Sir W. Batten did give me three bottles of his Epsom water, which I drank and I found myself mightily cooled with them and refreshed." Three years later Pepys made a Sunday's excursion to the gay town, getting up at 4 A. M. to get ready, and setting out shortly after five o'clock with his wife in a coach and four horses, and provided "with bottles of wine and beer, and some cold fowl." Reaching Epsom at eight o'clock, he went to the well and drank four pints of the water. Then, off to the King's Head, where he hears "that my Lord Buckhurst and Nelly are lodged at the next house. . . . Poor girl! I pity her!" The popularity of the place became very great. Toland, who wrote an account of it at the beginning of the eighteenth century, says that on a Sunday evening he counted sixty coaches in a ring. The New Inn Tavern was thought to be one of the largest in England. At that time the visitors must have

been of a somewhat mixed character, as we are told that one of the elegant amusements consisted in trying to catch a pig by the tail. By this time the mineral water and its virtues had begun to be somewhat of a secondary consideration with those who frequented what had become quite a gay and lively town.

An enterprising apothecary, named Livingstone or Levingstern, realized this fact, and thought he saw a way to make a fortune. He accordingly bought, in 1706, a piece of land about half a mile from the Old Wells, and, having sunk a well, built in connection with it a large house with conveniences for dancing and all kinds of games of chance. He also erected shops for jewelers, milliners, and other trades which appealed to the fashionable folk of the day. Thus, by means of concerts, balls, and facilities for gambling, this apothecary attracted the people from the old well to the new one. Unfortunately, this scheming benefactor overreached himself, and in 1727 he purchased the lease of the old establishment, closed the well and killed the goose that laid the golden eggs, inasmuch as the new well did not possess the cathartic virtues of the old one, and Livingstone discovered that the attractions of his fashionable establishment were really only accessory to the healing qualities of the *sal catharticum*.

Notwithstanding this blow to the prosperity of Epsom determined efforts were made to retain the patronage of the gay and fashionable crowd of London. Some queer expedients were resorted to for doing this, and perhaps one of the strangest was the engagement entered into by the authorities of the town with Mrs. Mapp, the notorious "bone-setter," or "shape mistress," as she was called. This fat, ugly, drunken woman haunted the fairs of the country, and acquired a great name as an expert in the replacing of dislocated limbs, which she appears to have done by reason of her great strength, rather than by dexterity. Her eccentricities added much to her fame, as did also her affected sobriquet of "Crazy Sally of Epsom." Her cures struck the townsfolk of Epsom as being so extraordinary that they thought they would be justified in endeavoring to stem the waning fortunes of the town by giving this female quack and ragamuffin a fee of one hundred guineas if she would continue her residence there for one year. She is said to have made twenty guineas a day by her "profession." In the *Gentleman's Magazine* for 1736, we are told that "Mrs. Mapp continues making extraordinary cures." She has "now set up an equipage, and on Sunday waited on



Her Majesty." Her maiden name was Sally Wallin; she married a footman of the name of Mapp, who, within a fortnight, soundly thrashed her two or three times, and then decamped with a hundred guineas and such other portable property as he could lay his hands on. The good lady's success withstood this experience. Once a week she visited London, riding there in her gorgeous chariot, drawn by four horses, and accompanied by servants in splendid liveries. On her return journey she brought with her, as trophies of honor, the crutches of the patients she had cured. Sometime or other it may be convenient to write of the London quacks, and then more may be said about this lady and her crazy career. At the present it will suffice to say that her fame became so great that Hogarth portrayed her evil physiognomy in the centre of the upper portion of the "Under-takers' Arms." A more brutal and sinister face it would be difficult to conceive; it is gross in the extreme, and the repulsiveness of it is heightened by a double squint towards the nose. Her companions in the picture—two equally notorious quacks—John Taylor and Joshua (Spot) Ward, are, by comparison, most humane and benevolent-looking gentlemen.

The account of the pamphlet would not be satisfactory if something further were not said about the *sal catharticum amarum*. Grew took out a patent in 1698 for the preparation of it from the Epsom spring; but, as Grew points out, it was known that other wells, as those of Barnet and Dulwich, yielded aperient waters. In 1700 two chemists, George and Francis Moulton, the latter being no doubt the translator of Grew's monograph, found themselves in possession of springs at Shooter's Hill, in Kent, from which they obtained considerable quantities of the purging salt; in fact, in certain seasons they obtained as much as two hundredweights a week. Their success called forth some harsh strictures from Quincy, the compiler of the "Compleat English Dispensatory." In referring to the translator he says: "But the avaricious craft of a certain Furnace-Philosopher could not let this useful discovery in natural knowledge rest under the Improvement and proper Use of Persons of Integrity." Quincy goes on to complain, "that what was first sold for one shilling an ounce, and could not honestly be made under, is now come to be sold for not much above thirty shillings per hundredweight, which does not much exceed three pence per pound." This is apparently where the shoe pinched. He indulged his pessimism too soon, as appears

from what happened about fifty years later (about 1760), when a certain Ingram, a surgeon, advertised real Epsom salts, obtained by evaporating the Epsom water, at as much as five shillings the ounce. How it came about that the Epsom salt came to be confused with the *sal mirabile* of Glauber (*hodie*, Glauber's salts), and how it came to be made from bittern at the salt works of Lymington, near Southampton, and at Newcastle, may be read at considerable length in Dr. James' "New Universal English Dispensatory" or in his "Medicinal Dictionary." The production at Epsom was given up quite early in the eighteenth century. Neumann says he visited Epsom in 1713 and "found no person there who could give any information about the preparation of the salt," and he goes on to say that "I inspissated myself an hundred quarts of the water, but scarcely obtained from them half an ounce of saline matter." The production of Epsom salts from bittern continued until Wm. Henry, of Manchester, took out a patent, in 1816, for the production of it from dolomite.

To return to Grew's tract—the second part deals, as has already been mentioned, with the Use of the Bitter Purging Salt, and in the second chapter is a formula which must be regarded as the parent of *Haustus Niger*, although it is only in the form of a so-called Apozem, and would be taken in rather larger doses than the regulation  $\mathfrak{ss}$ . or  $\mathfrak{ss}$ ii. The formula reads in the translation:

Take Spring Water four Pints, Mace a Dram, Senna three Drams, boil them gently and add of the Bitter Purging Salt an Ounce, Flakey-Manna an Ounce and half, or two Ounces, and strain it.

The final chapter deals with the Abuse of Bitter Waters and their Salts.

It might be interesting to compare the work of Nehemiah Grew and Stephen Hales, inasmuch as they both concerned themselves with the anatomy and physiology of plants, and both attempted to find a means of making sea water into fresh water. Grew's publication on "Sea Water made Fresh" appeared in 1684, and went into about ten English editions as well as into French and Italian ones. This anticipated Hales' book by about half a century. Grew's link with pharmacy, however, is his discovery of the purgative salt of the Epsom Spring.

## ELDER FLOWERS.\*

By E. M. HOLMES, F. L. S.

July is the month when the elder is in full blossom, and attention may, I think, be reasonably directed at the present moment to the importance of this abundant shrub for the herb industry. It is surprising how little attention is paid to the cultivation and propagation of this plant in Great Britain, whilst the flowers dried, or salted fresh, as well as dried berries and the juice of the fresh berries are imported by the ton. This may possibly be because the price of Continental produce is less than that of this country. Whether this is due to labor being cheaper abroad, or to the collection of material being facilitated abroad by methods of collection with less expenditure of time and labor, I have at present no evidence. I have, however, frequently been asked to procure elder flowers salted by the ton, and elderberry juice by the gallon, and dried elderberries and fresh leaves by the hundredweight. Dried elder flowers are, I know, imported by the ton from the Continent, of good color and free from stalks, at half the price that the English-grown flowers cost in this country, although the Continental article has to pay freight in addition to the cost of collection.

The question therefore arises whether anything can be done to lower the price of the English produce so as to enable it to compete with the foreign article. I venture to offer (for the consideration of the Royal Agricultural Society) some suggestions with this point in view. The elder tree, which is allowed to grow in the wild state here and there in hedges all over the country, necessitates a considerable waste of time and labor in going from place to place and in trying to pull down the branches that are out of reach, and there is, therefore, a tendency to pick all the bunches, whether the flowers are fully out or not. This labor and time might be saved by *cultivating the bush as a hedge* around gardens and fields, pruned after fruiting is over down to about six feet, so that the flowers and fruit may be within reach. At present hedges are allowed to be formed of many useless plants, and the space so wasted might be utilized also by forming hedges on chalk or limestone soils of female buckthorn plants, the berries of which there is the same difficulty in collecting. There are other points in connection with the elder to which atten-

\*Reprinted from the *Pharm. Journ and Pharm.*, June, 1921.

tion may be directed. The flowers open early in July and last in abundance only for about three weeks, during which time only it pays to collect them. The bunches of flowers do not open all the buds at once, and it needs a little judgment to collect those on which the majority of the corollas are expanded, leaving those in bud for a subsequent collection or for forming fruit. When the flower bunches are collected, if placed on the floor in heaps they soon heat and turn black, and care is necessary to spread them out on a *clean* floor, or on trays or shelves, so that the ripe corollas can be easily collected as soon as they fall off, which they easily do when only a very slight heating takes place. The separation can easily be done by the use of a coarse sieve, the bunches with unopened flowers being returned to their places for a second operation. Some buyers like to distil the flowers as soon as gathered for elder-flower water, but for the distillation at more convenient times the flowers are salted, 1 lb. of salt being added to 2 lb. of flowers. For the distillation of essential oil, for which there is a demand for the flavoring of the more delicate white wines, it is absolutely necessary to have no stalks and no flowers that have turned brown, as this spoils the delicacy of the flavor. Clean barrels or other containers are usually supplied by the buyer, as it is not always possible to get them in small country villages. These should be sent about the middle of May whenever salted flowers are wanted, so as to be clean and *ready for use as soon as the flowers are ready*. When the barrels are filled to the top with salt and flowers, no more should be added, but the flowers allowed to sink down, the top tided over with clean Hessian canvas, and labelled "To be kept upright."

With regard to the collection, it must be remembered that at the rate of 1 cwt. per day only  $1\frac{1}{2}$  tons can be collected during the month, and a month is practically the limit of time for collection of the flowers. Under present conditions, local advertisement is necessary to ensure a sufficient supply being brought in, accompanied by a printed notice to the effect that flowers turned brownish cannot be accepted. Fresh flowers are sometimes required for immediate distillation. In such cases they should be sent in sacks containing not more than 20 lb., and so loosely packed as to allow freedom from pressure by not tying up the sack too tightly, so as to permit movement of the flowers inside and avoidance of heating, and they should be labelled, "By passenger train, at owner's risk rate. Perishable." Or, by arrangement with the buyer, sacks containing 10 lb. each,

are more likely to arrive in good condition if sent by parcel post, under present conditions.

Elder leaves are best gathered when the green color is fully developed, as they are chiefly used for making green oil ointment, "Ol. Sambuci virid."

Elderberries for drying should be collected as soon as the berries assume a reddish-purple color or they soften too much in drying. The short stalks need sifting out when they are brittle after drying.

For elderberry juice the ripest berries should be used, and to the juice 1 per cent. of formic acid is added. The juice is probably most conveniently obtained in country villages by the use of a cleaned cider press. The juice is chiefly used by wholesale manufacturers of elderberry wine. The formic acid can be got rid of by boiling the juice when required for making the wine.

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## WHAT IS AN ANTIBODY?\*

Within the last few years the words "antigen" and "antibody" have become terms in the vocabulary of practical medicine as well as in the science of immunology. Discussion of the general phenomena of immunity can scarcely be carried on without reference to them. An antigen is a substance which, on introduction into the body in proper amounts and under suitable conditions, induces the formation of a special antagonistic substance, the antibody. At the present moment there are scarcely any well authenticated exceptions to the general rule that every soluble complete protein may serve in at least some degree as an antigen. With respect to the cleavage products of the proteins the evidence of their antigenic properties is at most debatable; certainly none of the amino-acids or simpler polypeptids, *i. e.*, amino-acid complexes, can serve as antigens. The alleged function of lipoids in this role is likewise not established. Karsner and Eckert<sup>1</sup> insist, in fact, that if lipoids are obtained from animal tissues, favorable results may be obtained; but in none of these experiments is it proved that the lipoids are entirely free from proteins. Far less is definitely known with respect to the nature of the manifold anti-

\*From *Jour. Amer. Med. Assoc.*, July 16, 1921.

<sup>1</sup> Karsner, H. T., and Ecker, E. E.: *The principles of Immunology*, Philadelphia, J. B. Lippincott Company, 1921, p. 22.

bodies. Diphtheria antitoxin, which has been studied longest in an intensive manner, has served as the prototype of this class of substances. There has been much evidence to indicate its close relationship or association with certain proteins, notably the globulins of the blood. It is not analogous to enzymes, if one may judge from the failure of antitoxin to be adsorbed by or removed from solution with a variety of indifferent precipitates. The large size or colloid character of the antibody molecule is shown by its comparative non-diffusibility. Recent studies by Huntoon, Masucci and Hannum have helped to narrow the field of investigation somewhat by indicating more clearly than heretofore that antibodies do not belong to that group of proteins usually classed as serum proteins. They showed, as others have previously indicated, that antibodies resist tryptic digestion—a fact which makes them unlike ordinary proteins. Antibodies, furthermore, do not manifest those biochemical reactions and transformations which are at present ascribed to the ill-defined euglobulin and pseudoglobulin fractions of the blood. Being insoluble in ether, they cannot be classed as lipoids or fats. By knowing more precisely what antibodies are not, we may hope to succeed better in the coming years in learning more adequately what they really are.

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#### A NEW METHOD FOR THE DETERMINATION OF CAFFEINE IN TEA AND COFFEE.\*

No samples of tea were examined during the past year for inspection purposes, but methods for the determination of caffeine were further studied and the results included in the report of the writer as Referee on tea to the Association of Official Agricultural Chemists at their annual meeting in November, 1920.

The Power and Chestnut method<sup>1</sup> was studied and recommended to the Association as an official method. The Stahlschmit method<sup>2</sup> which is now tentative was further modified<sup>3</sup> so that caffeine residues of a high degree of purity can be obtained. A new procedure

\*From the Connecticut Agricultural Experiment Station Bulletin No. 227, Feb., 1921.

<sup>1</sup> *Jour. Am. Chem. Soc.*, 41, 1300.

<sup>2</sup> *Jour. A. O. A. C.* 2, 3, 332.

<sup>3</sup> By C. E. Shepard and the writer.

was also evolved<sup>4</sup>, based upon the two methods just mentioned and the Deker<sup>5</sup> method, which has thus far been found to give satisfactory results and which is rapid and simple to manipulate. The two a view to the adoption of one or the other as an optional official method.

The proposed new method is as follows:

*Preparation of sample:* Grind the tea to pass a 1/25 inch sieve.

*Assay:* To 5 grams of material in a 500 cc. graduated flask add 10 grams of heavy magnesium oxide and 200 cc. of distilled water. Boil gently over a low flame for two hours using a small bore glass tube 30 inches long as a condenser. Cool, dilute to volume and filter through a dry paper. Take an aliquot of 300 cc., equivalent to 3 grams of original material in an Erlenmeyer flask of 1,000 cc. capacity, add 10 cc. of a 10 per cent. solution of sulphuric acid and evaporate by gentle boiling until the volume is reduced to about 100 cc. Filter into a separatory funnel washing the flask with small portions of 1 per cent. sulphuric acid and shake out six times with chloroform using 25, 20, 15, 10, 10, 10 cc. portions. Treat the combined extracts with 5 cc. of a 1 per cent. solution of potassium hydroxide. When the liquids have completely separated draw off the chloroform layer into a suitable flask or beaker. Wash the alkaline solution in the separatory with two portions of chloroform of 10 cc. each and unite the washings with the main bulk of extract. Evaporate or distill off the chloroform to small bulk, transfer to a tared flask, evaporate to dryness, and further dry in a water oven at 100° C. to constant weight.

If desired, transfer the residue thus obtained to a digestion flask with successive small portions of sulphuric acid and determine nitrogen by the Kjeldahl method, calculating caffeine from nitrogen by the factor 3.464.

The results obtained by the several methods are given in Table XIII.

<sup>4</sup> By R. E. Andrew and the writer.

<sup>5</sup> Chem. Zentr. 1, 1, 62, 1903.

TABLE XIII.—CAFFEINE IN TEA.

	<i>Stahlschmidt Method</i>		<i>Power and Chestnut Method</i>		<i>Proposed Method</i>	
	<i>By Weight.</i>	<i>From N.</i>	<i>By Weight.</i>	<i>From N.</i>	<i>By Weight.</i>	<i>From N.</i>
	%	%	%	%	%	%
Black tea, 4	2.83	2.81	3.06	2.99	2.98	2.86
	2.89	2.87	3.05	3.03	2.94	2.87
	2.86	2.84	3.05	2.95	2.92	2.82
	....	....	....	....	2.80 <sup>1</sup>	2.80 <sup>1</sup>
	....	....	....	....	2.84 <sup>1</sup>	2.80 <sup>1</sup>
Green tea, 5	1.64	1.63	1.61	1.55	1.70	1.61
	1.65	1.59	1.69	1.60	1.66	1.58
	....	....	....	....	1.77	1.66
	....	....	....	....	1.57 <sup>1</sup>	1.52 <sup>1</sup>
	....	....	....	....	1.62 <sup>1</sup>	1.57 <sup>1</sup>
Green tea, 9	2.09 <sup>2</sup>	1.94	2.12	2.01	2.14	2.08
Black tea, 10	2.71 <sup>2</sup>	2.63	2.69	2.67	2.62	2.62
Black tea, 12	3.10 <sup>2</sup>	2.96	3.20	3.12	3.00	2.93
	....	....	....	....	3.15	3.03
	....	....	....	....	3.12	2.99

Satisfactory methods<sup>3</sup> have been worked out for caffeine in coffee but we have been interested to try the proposed method on that substance. In two samples tried we have obtained the following results:

<i>Sample No.</i>	<i>Power and Chestnut Method.</i>		<i>Proposed Method.</i>	
	<i>By Weight.</i>	<i>From N.</i>	<i>By Weight.</i>	<i>From N.</i>
	%	%	%	%
15409	1.51	1.47	....	....
	1.49	1.45	1.61	1.49
15410	0.21	0.17	....	....
	0.21	0.18	0.28	0.24

Sample 15410 was a decaffeinated product. The results suggest that the method is probably applicable also to coffee.

<sup>1</sup> Results by H. A. Lepper.

<sup>2</sup> Not purified by treatment with potassium hydroxide.

<sup>3</sup> H. A. Lepper, A. O. A. C. Referee on Coffee, Report of 1920.



## SCIENTIFIC AND TECHNICAL ABSTRACTS

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A NEW DIGITALIS BODY.—From experiments performed on cats, using the Hatcher digitalis-ouabain method, it is assumed that there is present in digitalis leaf a substance having a characteristic digitalis-like action, but the effect of which is extremely fleeting. This assumption is deduced from the fact that it requires a much smaller amount of a digitalis preparation per kg. body weight to produce death, injected intravenously into cats during the passage of a few minutes than when the injection is carried out over a period of hours. In the case of digitoxin, the effect is exactly the opposite.

The statement is made that Hatcher has found the same thing to be true of his chloroform soluble fraction of the drug, but in a more pronounced degree.—M. S. Dooley, *Journ. of Pharm. and Exper. Therapeutics*, 17, 277, 1921.

W. J. McG.

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CHENOPODIUM AMBROSIODES.—The genus *Chenopodium* embraces sixty to eighty widely distributed species, but only two, viz., *C. Quinoa*, Linn., and *C. purpurascens*, Jacq., have attained any importance as food substances. The former produces the starchy quinoa seeds of Chili, and the latter has been cultivated in France for its leaves, which are used as a substitute for spinach. *C. ambrosioides*, Linn., is the only one of medicinal importance. It is probably a native of Mexico, but has spread all over North and South America; it occurs also in Africa, India, etc., in numerous varieties. It has been used for colic and dysentery, but its chief value is as an anthelmintic. Usually the volatile oil distilled from the plant is now employed. It is recommended for cultivation in France and the French Colonies; in the latter case the properties of the drug should be made known to the natives.—A. Chevalier, *Bull. d. Sc. Pharm.*, 28, 129; through *Pharm. Journ. and Pharm.*, June, 1921.

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ACTIVE CONSTITUENTS OF SHEPHERD'S PURSE.—The authors have shown that extracts of this drug (*Capsella Bursa-pastoris*) contain a substance which causes a very marked depression of the blood

pressure, and also a product which causes a rise in the blood pressure, and which is carried down by the precipitate when mercuric chloride is added to the extract. The latter substance is probably tyramine, but it could not be identified with certainty. It is very improbable that histamine is present. No evidence of the presence of an alkaloid was obtained. The choline bases were obtained directly by precipitation with alcoholic platinum chloride solution, and the following method of evaluating the extract is based on this observation: Five cc. of the liquid extract (1 in 1) is mixed with 12 cc. of alcohol and 20-25 cc. of 1 per cent. alcoholic solution of platinum chloride. The precipitate is filtered after one or two days, dried, and subsequently extracted on the filter with hot water, the impurities remaining on the filter. The filtrate is evaporated in a tared dish, and if necessary again filtered. A good sample of the drug should yield at least 0.2 gm. of platinum compounds, the purity of which is controlled by observation of the melting point.—Boruttau and Capenberg, *Arch. Pharm.*, 1921, 259, 33-52; through *Pharm. Journ. and Pharm.*, June, 1921.

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BENZYL ESTERS OF THE HIGHER FATTY ACIDS.—The authors have shown that the benzyl esters of the higher fatty acids may readily be prepared, either by the action of benzyl alcohol on the acid chloride, or by the action of benzyl chloride on the alkali salt of the fatty acid dissolved in excess of the fatty acid. These esters are tasteless and odorless, and have an antispasmodic action. They are more readily hydrolyzed by lipase than are the benzyl esters of the aromatic acids. Bye (*Journ. Ind. Eng. Chem.*, 1921, 13, 217-218) has prepared benzyl succinate by heating succinic acid with benzyl alcohol. It forms snow-white crystals, and is practically non-toxic. This substance may be used medicinally with advantage in any conditions where the use of benzyl benzoate is indicated.—Shoule and Row, *J. Amer. Chem. Soc.*, 1921, 43, 361-365.

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A TEST FOR THE ADULTERATION OF OLIVE OIL.—M. Ernest Milieu in a paper presented to the French Academy of Sciences, recommends the following method for detecting the presence of small amounts of cottonseed oil in olive oil. The fatty acids of the oil are separated in the usual manner and dissolved in three times their volume of 90° alcohol. The solution is then placed on a water bath and

1-10 of its volume of 3 per cent. silver nitrate solution is added. After a few minutes' ebullition there will be a black paste-like scum of fatty acids come to the surface, if cottonseed oil is present. This reaction is due to reduction of the nitrate and does not take place with the fatty acids of pure olive oil. With this method 1 per cent. of cottonseed oil in the olive oil can be detected. *Perfumery and Ess. Oil Record*.

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THE USE OF EDESTIN IN DETERMINING THE PROTEOLYTIC ACTIVITY OF PEPSIN.—The United States Pharmacopœia method is the only official one in the United States for the assay of pepsin. This method is not proving satisfactory. Edestin, the protein of hempseed, has been used to supply the protein in clinical methods worked out by others for the determination of proteolytic activity, and since it is easily and cheaply prepared the author considers that it may advantageously be used in the assay of commercial pepsin.

Edestin is prepared by extracting nearly fat-free hempseed meal with 5 per cent. sodium chloride solution at 65°. The edestin, which separates on cooling the filtered extract, is recrystallized from the same medium. The nitrogen content of the washed and air-dried edestin is carefully determined, and this multiplied by 5.35 is adopted as giving the percentage of edestin in the preparation. From this the amount of preparation to supply a given amount of edestin is calculated.

For the assay a 1 per cent. solution of edestin in 0.1 N hydrochloric acid is placed in test tubes arranged in a constant temperature bath at 37.5° in increments of 0.25 cc., beginning with 0.25 cc. in tube 1. Tubes 4, 5 and 6 receive 1 cc. To the edestin solution is added 0.1 N hydrochloric acid in decrements of 0.25 cc., beginning with 0.75 cc. in tube 1, thus adjusting the volume in each tube to 1 cc. One cc. of 10 per cent. sodium chloride solution is added to each tube to precipitate the protein. This is followed by the addition of 1 cc. of 1 per cent. solution of the pepsin to be tested in 0.05 N hydrochloric acid. The time from the beginning of the addition of pepsin until the protein is completely liquefied is noted. If the volume of substrate is represented by  $s$ , and the time of digestion by  $t$ , then  $t/s$  is nearly constant. It is better to adopt the mean  $t/s$  for all tubes as the constant. The comparison of the proteolytic activity of different pepsins resolves itself into a comparison of the constants thus obtained.—*J. Biol. Chem.*, 46 (1921): 119; through *Journ. Frank. Inst.*

**RAPID DETECTION OF MORPHINE IN THE TOXICOLOGICAL ANALYSIS OF VISCERA.**—By means of the following method morphine was detected in the viscera after ingestion by the subject of only 0.002 gram. One hundred and twenty grams of viscera are mixed with magnesia to a compact paste, which is completely dehydrated on the water bath. The powdered residue is boiled with acetone, and the filtered extract treated with 2-3 cc. of water and a few drops of acetic acid. The liquid is again filtered and evaporated on the water bath. The residue containing the morphine is purified by treatment with 5% acetic acid, filtration, and extraction with boiling chloroform, after addition of excess of ammonia.—Through the *Pract. Druggist*.

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**CONSTITUENTS OF SIAM BENZOIN.**—The author has isolated *d*-siaresinolic acid by treating the crude benzoin with aqueous solution of sodium hydroxide (4-5 per cent.), and recrystallizing the sodium *d*-siaresinolate from alcohol. The free acid has a specific rotation at 25° of + 37.793 in alcoholic solution, and melts at 260° C. It does not contain a methyl group, and plays no part in the gradual discoloration suffered by the resin when preserved. The potassium salt crystallizes in needles, which dissolve freely in water and alcohol. The name *l*-prabangic acid is proposed for the substance  $C_{27}H_{40}O_4$  isolated by Zinke and Lieb by the oxidation of *d*-siaresinolic acid by chromic acid in acetic acid solution. Lubanyl benzoate is described by the same author as the substance which exhibits a series of color changes analogous to those shown by the crude resin. It crystallizes in plates melting at 72.8° C., and contains one methoxy group. It readily loses benzoic acid when heated to 120°-140° C., and on further rise of temperature emits and an odor of carnations and subsequently of guaiacol. It is optically inactive. The benzoate is very readily hydrolyzed either in acid or alkaline solution, but the isolation of lubanol itself in the pure condition has been impossible owing to its susceptibility to change. Lubanol is probably identical with, or closely related to, coniferyl alcohol.—Reinitzer, *Archiv. Pharm.*, 1921, 259, 1-6, 60-69; through *Pharm. Journ. and Pharm.*, June, 1921.

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**VOLATILE OIL OF PIMENTA JAMAICENSIS (AMOMIS JAMAICENSIS).**—The oil derived from the leaves of the wild pimento of Jamaica have been investigated by the author. It has an odor resembling

that of spike lavender oil, and is pale yellow in color. The leaves yielded 0.49 per cent. of volatile oil, having the following constants:

Specific gravity (15° C.) .....	0.8895
Optical rotation (22°) .....	6°
Refractive index (20°) .....	1.471
Acid value .....	2.4
Ester value .....	4.2
Ester value after acetylation .....	129.4

It was soluble in 2.5 volumes of 70 per cent. alcohol at 15° C., becoming cloudy with 6 volumes. Traces of caproic and acetic acids were found and about 0.1 per cent. of an aldehyde, which was not identified. A phenol was extracted which amounted to about 0.1 per cent. of the original oil. It gave a reddish-violet coloration with ferric chloride, but no evidence of the presence of eugenol was obtained. On fractionation about 15 per cent. of cineol was obtained, which gave an iodole compound melting with decomposition at 116° C. Two terpenes were separated, one giving the characteristic nitrite of  $\alpha$ -phellandrene, melting at 112-113° C.; the other furnished a tetrabromide, melting at 124° C., indicating the presence of dipentene. From the fraction boiling at 190-205° a liquid having the odor and characters of linalool was obtained, which on oxidation with chromic acid yielded citral. Geraniol was isolated from the fraction boiling at 220-235°, which was identified by conversion into the acid phthalic ester, and by oxidation to citral. The diphenylurethane, melting at 80-81°, was also prepared. The last fraction boiling above 235° was brown and rather viscous. By distillation over sodium under reduced pressure a colorless oil was obtained having a specific gravity of 0.9320 and boiling between 245-290°, but the amount of oil was too small to permit further investigation of this product, which probably contained sesquiterpenes. The composition of this oil is, therefore, quite different from the oils of *Pimenta* species previously examined, which include oil of pimento fruits, from *Pimenta officinalis*, oil of bay leaves, from *Pimenta acris*, and two varieties of *P. acris*, one containing citral and the other having a characteristic odor of anise.—O. D. Roberts, *Journ. Soc. Chem. Ind.*, 40, 9, 491; through *Pharm. Journ. and Pharm.*, June, 1921.

## MEDICAL AND PHARMACEUTICAL NOTES

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FORMALINE IN URINE.—Dr. E. Pittarelli (*Lancet*, II., 1920, p. 1267) recently described a test for formaline in urine. The practical application is as follows: To 25-30 cc. of urine (acid or made acid) 10-12 drops of a 1 per cent. solution of phenylhydrazine is added and the mixture heated to boiling. After a few minutes 5-6 drops of a 1 per cent. solution of metol and 3-4 drops of a 25 per cent. solution of caustic soda are added, when a crimson color is produced, which, on the addition of magnesian salt, assumes a decided purple color. The crimson is stated to be appreciable to a 1 in 100,000 solution of formalin, and the purple tint increases the sensibility still further.—Through *Chem. and Drug.*, June, 1921.

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TREATMENT OF POISON OAK DERMATITIS.—Alderson and Pruett report thirty-four cases in which treatment consisted of the injection of 1 cc. poison oak extract into the gluteus or deltoid. Almost invariably one intramuscular injection is followed by great relief of the local symptoms; swelling and itching particularly begin to subside within twenty-four hours. There is not much local irritation as a rule, but at times where some of the fluid has worked its way along the track of the needle, a painful indurated nodule appears and is slow in subsiding. Some of the patients seem to have become immune.—*Cal. State Journ. of Med.*, through *Journ. A. M. A.*, June, 1921.

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PREPARATION OF STERILE IODOFORM EMULSIONS.—According to Blomberg, sterile and stable iodoform emulsions may be made by the following method: Cover two portions (60 and 40 gm.) of iodoform with 20 and 25 cc. respectively of an ethyl alcohol and ether mixture containing 4 parts of ether to 1 of alcohol. Let this mixture stand in the dark for 12 hours and then evaporate in a vacuum desiccator. Dissolve the 40 gm. portion in a liter of sterile olive oil at 55° C. Grind the 60 gm. portion as finely as possible in a sterile mortar. Add it to the solution and shake thoroughly. No crystalline iodoform will precipitate from this emulsion.—*Pharm. Weekblad*, through *Chem. Abs.*

**BLACK DRAUGHT.**—One of the earliest of the popular laxative potions was devised by Mannagetta, an Italian physician, at the court of the Emperor Rudolph II, about 1600. His prescription became popular under the title of aqua or potio laxativa viennensis and was popularly known in Germany as "Wiener Trank." The formula called for 1 ounce of senna, 6 drams of currants, 2 drams of coriander seeds, and  $2\frac{1}{2}$  drams of cream of tartar. These ingredients were packed in a bag and suspended in hot water for a night. In the morning the liquor was strained off and 5 ounces of manna and 2 drams of cream of tartar added. The dose was from 3 to 4 ounces. Various modifications of this appeared in the various formularies, the juice and peel of lemon being included in some. According to Wootton the term "black draught" first appeared in Paris' "Pharmacologie" in 1824. In Brande's "Materia Medica and Pharmacy" in 1839 the term "black dose" was given. In 1885 the synonym "black draught" appeared. Dorvault in his "L'Officine" gives the formula for a compound senna mixture under the title of "Potion Noire Anglaise."—Through the *Merrell Messenger*.

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**OIL OF BRICKS.**—In the earlier pharmacopœias of London and Edinburgh, as well as in several other pharmacopœias of the eighteenth century a formula was given for the preparation of "oil of bricks." According to the London Pharmacopœia of 1746 we are told to heat bricks red hot and quench them in olive oil until they had soaked up all the oil. They were then broken up into small pieces, put into a retort, heated on a sandbath and distilled, producing a mixture of empyreumatic oil and water which was known as oil of bricks, oleum sanctum, oleum divinum, and oleum benedictum.—The *Merrell Messenger*.

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**SOLVENT FOR ACETYL-SALICYLIC ACID.**—Acetyl-salicylic acid (aspirin) is practically insoluble in water, and though soluble in alcohol such a solution is not generally suitable for administration. It is therefore usually given in tablets or cachets. Solution may be effected by addition of sodium bicarbonate, but as the resulting solution is merely a mixture of sodium acetate and sodium salicylate, this method is not admissible. It is said that sodium citrate will dissolve acetyl-salicylic acid without dissociation: for each grain of

aspirin 4 grains of sodium citrate should be added. Such a solution, flavored with syrup of lemon, is suitable for administration to children. Through the *Prescriber*, June, 1921.

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FOODS AND VITAMINES.—The recent study of the vitamins has modified our conception of what a perfect food should be. From a chemical point of view it should provide sufficient calories to maintain the warmth of the body, and produce energy and also sufficient salts and proteins to furnish an adequate proportion of the various indispensable amino-acids. Biologically it should contain a sufficient amount of vitamins to ensure growth in the young and equilibrium in the adult. Physically it should contain cellulose corresponding in volume to the length of the intestine. The authors have examined a number of advertised foods, and found that many fall short of these requirements. White rats were employed as test animals. Five advertised infants' foods were insufficient to maintain life, and the rats fed on them exclusively died in periods varying from ten to forty days. Other foods had the same result, but maintained life longer; while others, again, maintained life, but were insufficient to allow of growth. Perrot and Lecoq consider their experiments prove that it is quite possible to produce foods that are not devoid of any one of the essential ingredients; in fact, three of those examined were of this nature. Manufacturers should have their foods tested, and remedy any deficiencies that may be shown to exist. Cereal proteins can be improved by the addition of animal proteins; the necessary ions which are often deficient are sodium, calcium, and chlorine; milk, eggs, beer yeast, cereal germs, etc., may be utilized as a source of vitamins.—Em. Perrot and R. Lecoq, *Bull. des Sciences Pharm.*, 28, 177; through *Pharm. Journ. and Pharm.*, June, 1921.

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ATROPINE SULPHATE FROM DATURA STRAMONIUM.—The authors have prepared atropine sulphate in crystalline form from stramonium herb by the following method: The ground plant was extracted with water containing 0.2 per cent. of sulphuric acid and 0.5 per cent. of formaldehyde; the percolate was treated with Fuller's earth, allowed to settle, and the sludge collected and dried at 50° C. The absorbed alkaloids were extracted with alcohol, using lime to obtain alkalinity; the extracts were acidified with acetic acid and concentrated first to 12 per cent. and then under reduced pressure to 2



per cent. of the original volume. This treatment was sufficient to convert all the hyoscyamine present into atropine. The solution was then rendered ammoniacal, the solution neutralized with sulphuric acid, evaporated to a syrup, and the latter while hot treated with acetone until precipitation almost commenced; on cooling atropine sulphate crystallized out.—Rhodehanel and Stuart, *Journ. Ind. and Eng. Chem.*, 1921, 13, 218-220.

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RESISTANCE OF ACONITINE TO PUTREFACTION.—A rat was killed by the subcutaneous injection of 2 mgms. of aconitine. The carcass was left to putrefy for several days in the air, then enclosed in a metal box, and buried for two months. The pulped viscera were then extracted with absolute alcohol, acidified with 10 per cent. of tartaric acid, and kept at 60° for fifteen minutes. The cooled liquid was filtered and distilled in vacuo. This extraction was twice repeated. The final residual extract was dissolved in water and filtered. It was then shaken out with ether while still acid. The ether was removed, and the aqueous portion was rendered faintly alkaline with sodium bicarbonate, and again shaken out with ether and with chloroform. The last extract was evaporated, and the residue dissolved in 10 per cent. acetic acid. This solution gave positive reactions with Mayer's and Nonti's reagents, had the characteristic numbing action on the tongue, and gave a violet color with a 4 per cent. solution of sodium phosphate in molybdic acid. No reaction for ptomaine was obtained by Brouardel and Boutmy's test. It is therefore concluded that aconitine is not destroyed by flood ferments; that it resists putrefaction for two months; that weak acids and alkalies should be used for its extraction; that it can then be characterized by the organoleptic test and by the phosphomolybdic color reaction. It is stated that crystalline aconitine gives no violet reaction with ordinary phosphoric acid, either hot or cold.—*Austra. Journ. of Pharm.*, April, 1921.

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SELECTED FROM AN ARTICLE ON DISPENSING IN THE PHARMACEUTICAL JOURNAL AND PHARMACIST, MARCH, 1921, BY A. B. GILMOUR.

#### A. B. C. LINIMENT.

With regard to A. B. C. Liniment, chemists frequently note on the prescription that for Lin. A. B. C. they have dispensed the British

Pharmaceutical Codex preparation, while others have noted that they dispensed the Royal Infirmary, Edinburgh, Pharmacopœia preparation.

A. B. C. Liniment is a synonym for the British Pharmaceutical Codex preparation *Linimentum Aconiti Compositum*, and is composed of:

Liniment of Aconite .....	2 parts
Liniment of Belladonna .....	2 parts
Chloroform .....	1 part

The British Pharmaceutical Codex states that this recipe is an improvement upon the forms of A. B. C. Liniment containing oil.

The Edinburgh Royal Infirmary Pharmacopœia *Linimentum A. B. C.* is composed of equal parts of Aconite Liniment, Belladonna Liniment, and Chloroform Liniment, and the recipe is the same as that stated in Martindale as being used in Guy's Hospital.

Martindale notes that while the olive oil in the Chloroform Liniment is not soluble in the other liniments, it is useful as a lubricant.

#### THE THREE SYRUPS.

As regards the three syrups:

The B. P. C. recipe is the same as that given in Martindale, and is equal parts of—

Syr. Ferri Phos. Co. c. Quin. et Strych.  
Syr. Hypo. Co.  
Syr. Ferri Phos. Co.

The Edinburgh Royal Infirmary recipe is:

Syr. Ferri Phos. Co. c. Quin. et Strych. ....	1 part
Syr. Hypo. Co. ....	1 part
Syr. Ferri Phos. Co. ....	2 parts

The recipe in the Pharmaceutical formulas is the same as the Edinburgh Royal Infirmary recipe, and it is interesting to note that two well-known makers of proprietary tablets also adopt the Edinburgh Royal Infirmary recipe.

LOTIO CALAMINÆ.

*The B. P. C. Recipe.*

Prepared Calamine .....	44 grains
Zinc Oxide .....	22 grains
Glycerin .....	24 minims
Diluted Rose Water .....to	1 ounce

*Edinburgh Royal Hospital for Sick Children.*

Prepared Calamine .....	80 grains
Zinc Oxide .....	40 grains
Glycerin .....	10 minims
Boric Acid .....	16 grains
Distilled Water .....to	1 ounce

*Royal Infirmary, Aberdeen.*

Prepared Calamine .....	30 grains
Zinc Oxide .....	30 grains
Starch .....	30 grains
Glycerin .....	60 minims
Water .....to	1 ounce

LOTIO PLUMBI CUM OPIO.

*The B. P. C. Recipe.*

Tincture of Opium .....	24 minims
Lead Lotion .....to	1 ounce

*Edinburgh Royal Infirmary.*

Lead Acetate .....	4 grains
Opium in powder .....	4 grains
Distilled Water .....to	1 ounce

*Edinburgh Royal Hospital for Sick Children.*

Lead Acetate .....	4 grains
Opium in powder .....	4 grains
Diluted Acetic Acid .....	4 minims
Water .....to	1 ounce

*Aberdeen Royal Infirmary.*

Lead Acetate .....	4 grains
Tincture of Opium .....	15 minims
Water .....	to 1 ounce

In the 17th Edition of Martindale's "Extra Pharmacopœia" the recipe for Lotio Plumbi et Opii is three minims of Tincture of Opium to one ounce of Dilute Lead Acetate Solution.

For Lotio Plumbi cum Opio chemists have also written on the prescription form the recipe which they dispensed, and the strength of both the Tincture of Opium and the Solution of Subacetate of Lead has varied as between chemist and chemist and the other recipes referred to.

LOTIO RUBRA.

*The B. P. C. Recipe.*

Zinc Sulph. ....	2 grains
Tr. Lavand. Co. ....	10 minims
Water .....	to 1 ounce

*Aberdeen Royal Infirmary.*

Zinc Sulph. ....	3 grains
Tr. Lavand. Co. ....	10 minims
Water .....	to 1 ounce

*Edinburgh Sick Children's Hospital.*

Zinc Sulph. ....	2 grains
Tinct. Cocci .....	2 minims
Water .....	to 1 ounce

*Aberdeen Royal Infirmary.*

Zinc Sulph. ....	1 grain
Tr. Lavand. Co. ....	15 minims
Water .....	to 1 ounce

MISTURA ALBA.

*The B. P. C. Recipe.*

Mag. Carb. Lev. ....	10 grains
Mag. Sulph. ....	60 grains
Aq. Menth. Pip. ....	to 1 ounce

*Edinburgh Royal Infirmary.*

Mag. Carb. Lev. ....	15 grains
Mag. Sulph. ....	40 grains
Aq. Menth. Pip. ....to	1 ounce

*Aberdeen Royal Infirmary.*

Mag. Carb. Pond. ....	10 grains
Mag. Sulph. ....	80 grains
Tr. Zingib. ....	10 minims
Water ....to	1 ounce

*Martindale.*

Mag. Carb. ....	15 grains
Mag. Sulph. ....	30 grains
Aq. M. P. ....to	1 ounce

*Squire.*

Mag. Carb. ....	10 grains
Mag. Sulph. ....	1 drachm
Aq. M. P. ....to	1 ounce

In connection with the recipe in Squire's Companion, the statement is made that that recipe is given in several hospital Pharmacopœias.

MISTURA AMMONIÆ CUM SENEGÆ.

*The B. P. C. Recipe.*

Carbonate of Ammonia ....	4 grains
Ipecac. Wine ....	10 minims
Inf. Senega ....	½ ounce
Water ....to	1 ounce

*Royal Infirmary, Edinburgh.*

*Mistura Ammonii et Senegæ Composita.*

Carbonate of Ammonia ....	10 grains
Comp. Tincture of Camphor ....	40 minims
Spirit of Chloroform ....	40 minims
Infusion of Senega ....to	1 ounce

*Recipe Dispensed by Chemist.*

Carbonate of Ammonia .....	10 grains
Spirit of Chloroform .....	10 minims
Bromide of Ammonia .....	15 grains
Antimonial Wine .....	20 minims
Syrup of Tolu .....	40 minims
Infusion of Senega .....to	1 ounce

The recipe in the British Pharmaceutical Codex is the same as the St. Thomas's Hospital recipe which is quoted in Squire's Companion.

MISTURA BISMUTHI CUM SODA.

*The B. P. C. Recipe.*

Sodium Bicarbonate .....	10 grains
Bismuth Mixture .....to	1 ounce
Glycerin of Bismuth Carbonate .....	30 minims
Water .....to	1 ounce

*Edinburgh Royal Infirmary.*

Bismuth Oxycarbonate .....	20 grains
Sodium Bicarbonate .....	20 grains
Glycerin .....	80 minims
Diluted Hydrocyanic Acid .....	5 minims
Comp. Tincture of Cardamoms .....	40 minims
Distilled Water .....to	1 ounce

MIST. RHEI CUM SODA.

*The B. P. C. Recipe.*

Powdered Rhubarb .....	5 grains
Bicarbonate of Soda .....	10 grains
Caraway Water .....to	1 ounce

*Recipes Dispensed by Chemists.*

(1)

Powdered Rhubarb .....	4 grains
Bicarbonate of Soda .....	20 grains
Carbonate of Ammonia .....	6 grains
Spirit of Chloroform .....	20 minims
Infusion of Gentian .....to	1 ounce

(2)

Comp. Rhubarb Powder .....	7½	grains
Bicarbonate of Soda .....	18¾	grains
Glycerin .....	1	drachm
Cinnamon Water .....	to 1	ounce

(3)

Comp. Rhubarb Powder .....	11¼	grains
Bicarbonate of Soda .....	15	grains
Spirit of Chloroform .....	15	minims
Glycerin .....	30	minims
Peppermint Water .....	to 1	ounce

The recipe in the British Pharmaceutical Codex is the same as the St. Thomas's Hospital recipe, which is quoted in Squire's Companion.

MIST. RHEI CO.

*The Edinburgh Royal Infirmary Recipe.*

Sulphate of Magnesia .....	40	grains
Tincture of Rhubarb .....	80	minims
Syrup of Ginger .....	40	minims
Distilled Water .....	to 1	ounce

*Recipe Dispensed by a Chemist.*

Compound Tincture of Rhubarb .....	30	minims
Bicarbonate of Soda .....	22½	grains
Glycerin .....	30	minims
Peppermint Water .....	to 1	ounce

UNGUENTUM ATROPINÆ.

With regard to Unguentum Atropinæ, I submit three prescriptions—

(1)

Atropine Ointment .....	1	ounce
Directions. The ointment.		

(2)

Atropine Ointment .....	½	ounce
No directions were given.		

A chemist supplied the following recipe:

Red Oxide of Mercury .....	2 grains
Atropine .....	1/2 grain
Lard .....	2 drachms
Soft Paraffin .....	2 drachms

(3)

Atropine Ointment ..... 1 ounce

Directions. Ointment for Eye.

Use three times a day.

SELECTED FROM AN ARTICLE ON DISPENSING IN THE BRITISH AND COLONIAL PHARMACIST, MARCH, 1921, BY HAROLD WYATT.

*Foreign Prescriptions*, though not of daily occurrence, are frequently handled in a great seaport town like Liverpool, and present difficulties mainly due to the language in which they are written or the preparations they call for:

*American.*—

Olei olivarum .....	5 iij.
Glycerini .....	5 v.
Fluidi extracti senegæ .....	5 iv.
Fluidi extracti pruni virginianæ .....	5 vi.
Fluidi extracti glycyrrhizæ .....	5 iv.
Spiritus vini gallici .....	ad 3 iv.

Fiat linctus.

This was dispensed minus the last ingredient, the owner being told to add this himself, a thing, as he said, he would scarcely have been able to do in "God's own country," owing to his countrymen's temperance notions.

Grammes.

Acidi arseniosi .....	.25
Strychninæ sulphatis .....	.20
Aloini .....	1.25
Pepsini (scales) .....	8.
Ferri redacti .....	10.
Quininæ bisulph. ....	10.

M. ft. capsule No. 100.



This is an illustration of the variety met with in American prescriptions and the number of capsules, etc., ordered.

Scandinavian scripts are usual, and as they are written in Latin, and usually in very good and legible caligraphy, they are easy to make out.

*Danish.*—

	Gramm.
Bromidi natrici	
Tinctura valerianæ .....	āā 15.
Phosphatis natrici .....	10.
Aquæ .....	ad 300.

i spisestre 3-4 gauge i dögnet.  
 (3 ss. three or four times a day.)

	Gramm.
Aqua ophthalmicæ boratæ .....	300

Fiat solutio.  
 This is sodii biboratis gr. 3.  
 Aquæ fœniculi gr. 297.

*French.*—

This one typical example of French prescribing in general will give a notion of what is ordinary.

	Grammes.
Benzoate de soude .....	2.
Terpene .....	1.
Sirop codeine .....	30.
*Eau de laurier cerise .....	15.
†Julep gommeux .....	150.
‡Teinture d'aconit .....	xxx gouttes

Faire deaux fois cette potion. (Send double this quantity.)

NOTE.—All ingredients in French prescriptions are weighed, liquids and solids, unless otherwise stated.

\*Cherry laurel water is often used in cough mixtures in France for the flavour mainly and also as a sedative.

†Julep gommeux, or potion gommeuse, consists of orange flower water, gum acacia, and syrup, see "B. P. C." and also "Squire."

‡Tincture of aconite 30 drops means 30 drops measured by a calibrated pipette, such as is ordered in the French Codex.

*Italian.*—

Solfato di zinco  
centigrammi dieci  
Cloridrato di cocaina  
centigrammi dieci  
Acqua destillata é  
sterilizzata  
grammi quindici

Fare collirio.

Dare schizzata conto gocce.

Grammis.

Zinci sulph. ....	.10
Cocainæ hydroch. ....	.10
Aquæ destillatæ (sterilised) ....	15.

Fiat collyrium.

Send an eye dropper.

*Italian.*—

Cianuro di idrargirico  
centigrammi venti  
Acqua distillata é  
sterilizzata  
grammi mille

Per lavature oculari

Grammes.

Hydrarg bicyanidi ....	.20
Aquæ distillatæ (sterilised) ....	1,000.

The eye wash.

The direction as to sterilising the water seems somewhat unnecessary in the presence of such a strong bactericide as mercuric cyanide.

*Russian Prescriptions* are invariably written in Latin—

Salis Pelletieri ....	0.5
Thiocol ....	0.1
Butyri cacao ....	1.5
Fiat globulus mitte 12.	

These pessaries were easy to make, but the identity of Pelletier's Salt was somewhat obscure. Examination of a pessary revealed the presence of a quinine salt, and therefore the soluble hydrochloride was used.

*Spanish Prescriptions* are usually written in Spanish, though at times one finds one in Latin. It is remarkable that the Latin nations seem to have almost entirely discarded the use of that language in prescriptions, which is to be deplored from every point of view:

	Gramos.
Glicerofosfato de cal.....	0.30
de sosa .....	0.20
de hierro.....	0.15
Polvo di paulinia .....	0.25
Hacer polvo.	

	Grammes.
Calcii glyceroph. ....	.30
Sodii " .....	.20
Ferri " .....	.15
Pulvi guarana .....	.25
Fiat pulvis.	

Bromuro de potaso .....	10.00
de sosa .....	10.00
de amonio .....	10.00
Jarabe C. N. A. ....	150.00
Hacer bebida.	

Tomese una eucharada de las de sopa al acostarsi y repitase si sea necesario.

Potass. brom. ....	
Sodii brom. ....	
Ammonii brom. ....	10 grammes
Syrupi aurantii .....	150.

Fiat mistura.

One tablespoonful at bedtime and repeat if required.

The contraction jarabe C. N. A. expanded is jarabe de corteza de naranja amarga syrup of bitter orange peel.

	Gramos.
Aceite de almendras .....	60.
Amoniaco puro .....	5.

Remedio para sabañones.

Oil of almonds .....	60 grammes
Ammonia liquid .....	5.

Chilblain Remedy.

Swiss.—

Guaiacol .....	0.05
Camphoræ .....	0.10
Iodoformi .....	0.01
Eucalptol .....	0.05

Fiat ampulla mitte xx.

These were simple to make, and were sent out made up to 1 cc. each with sterilised almond oil.

*Roumania.*—These are mostly written in French—at any rate, those we get from Roumanian ports—are of a distinctly French character, containing plenty of syrups and medicated wines, caffeine and glycerophosphates, as in the following example:

	Grammes.
Vin de quinquina .....	200
Vin de malaga .....	150
Glicerina neutra .....	150
	Centigrammes.
Arsenit de sodii .....	.10
Glicerofosfat de calce .....	10.
Tra nuca vomica .....	} āā
Kola .....	
Koka .....	
	5.

## NEWS ITEMS AND PERSONAL NOTES

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A GRANT FOR RESEARCH.—The American Pharmaceutical Association has available a sum amounting to about \$360, which will be expended after October 1, 1921, for the encouragement of research.

Investigators desiring financial aid in their work will communicate before September 1st with Prof. H. V. Arny, Chairman A. Ph. A. Research Committee, 115 West Sixty-eighth Street, New York, giving their past record and outlining the particular line of work for which the grant is desired.

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PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE NOW HAS BOTANIC GARDEN.—At a meeting of the Philadelphia College of Pharmacy, held on June 27th, a resolution was adopted, by a standing vote, to accept the offer of the H. K. Mulford Company of the use of a tract of land adjoining the Mulford Biological Laboratories, Glenolden, as a botanical garden.

The site is ideal for the purpose, lying as it does in the Valley of the Delaware, the soil and climatic conditions being especially favorable to the cultivation of medicinal plants.

Adjoining the original house on the grounds, which is a relic of Colonial times, is an old-fashioned garden, which is devoted to the cultivation of medicinal plants. This will be reserved for the College, as well as an open tract of land and a section of woodland so that the plants requiring partial shade, such as Aconite, Golden Seal, etc., can be cultivated.

In addition, the College will have the use of the greenhouse, implements, plant materials, hot and cold frames of the Mulford Company, who will also undertake the rough work such as the ploughing and preparation of the soil.

The direction of the work will be under Prof. H. W. Youngken, who will have the collaboration of Dr. Githens, Chief Botanist of the H. K. Mulford Company.

This department will be known as the Botanic Garden of the Philadelphia College of Pharmacy and Science, and will add greatly to the scope of that institution in giving practical training on botany, particularly as applied to medicinal plants,

DR. ROBERT P. FISCHELIS IS ELECTED DEAN OF THE NEW JERSEY COLLEGE OF PHARMACY.—At a meeting of the Board of Trustees of the New Jersey College of Pharmacy held June 29, 1921, Dr. Robert P. Fischelis was unanimously elected Dean and Professor of Practical and Commercial Pharmacy in that institution. He succeeds Dr. P. E. Hommell who has been made Dean Emeritus, and who will continue as Professor of Materia Medica, Botany and Physiology.

Dr. Fischelis will continue his work as a consulting chemist with offices in the Metropolitan Building, New York City, and will probably continue his lectures on Commercial Pharmacy in the Philadelphia College of Pharmacy and Science, with whose faculty he has been associated since the merger of the Medicochirurgical College Pharmacy Department with the Philadelphia College of Pharmacy and Science.

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## BOOK REVIEWS

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"THE ELEMENTS OF VEGETABLE HISTOLOGY." By C. W. BALLARD. John Wiley & Sons, Inc., New York, 1921; 46 pp., 75 illustrations.

The text covers to some extent the subject of microtechnique (involving the principles of infiltration, cutting, staining, etc.), the microscope, the plant cell and its contents, the covering supporting and conducting tissues and the tissues of synthesis. There also appear chapters on the root, stem, leaf, flower, fruit and seed. At the rear of the volume is a chapter on the various accessories of the microscope such as the mechanical stage the ocular micrometer, the camera lucida, etc., and lastly, there follows an appendix of formulæ, table of magnifications, etc.

The text shows a number of weaknesses. In the first place, there is a lack of clarity on certain points. Second, there is a dearth of suitable pharmacognostical illustrations and references. And finally many of the illustrations present (excepting those which have been

borrowed) are of too poor a quality to occupy the positions they hold.

On the other hand the simplicity of style is much in favor of the beginner who will not be burdened by the intricacies of so vast and difficult a field as botany. The author has, however, in trying to reduce facts to their lowest terms, here and there sacrificed comprehensive understanding for brevity.

At the present time, therefore, it seems that while the book is not as valuable as some, it should, nevertheless, serve as a nucleus for greater achievement.

M. S. DUNN.

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"ANALYST'S LABORATORY COMPANION." By ALFRED E. JOHNSON, B. Sc. Lond. Fifth Edition. P. Blakiston's Son & Co., Philadelphia, publishers; 176 pages. Price, \$3.50 net.

This book, as the title would indicate, is intended as an aid to the laboratory worker. In this edition the author has enlarged upon and revised several of the important features of previous editions and presents to the analyst a valuable and up-to-date collection of tables and data.

When one considers that about seventy separate headings are listed among the contents of this little volume he realizes how compact and concise a book of this size must be. Practically all of the more important and useful tables that are required in laboratory routine are given. Among these are tables of the international atomic weights for 1921, logarithms, densities of gases, gravimetric and volumetric factors, corrections for volumes of gases, volume and density of water at different temperatures, Baume's hydrometers, strength of hydrochloric, nitric and sulphuric acids of different densities, tables required for water analysis, for phosphates, for the conversion of nitrogen into ammonia, for the Kjeldahl process, thermometric tables, alcoholometric tables and tables of constants for oils, fats and waxes. There are also useful tables on freezing mixtures, melting points of metals, reciprocals of numbers, percentage compositions of commonly occurring compounds with formulæ and molecular weights, densities of elements and common substances.

strengths of saturated solutions of some of the common salts, beer analysis, the specific rotary power of carbohydrates, milk analysis, and a table showing the percentage of chicory with coffee from the percentage of aqueous extract.

In addition to these several explanatory notes are given on volumetric solutions, logarithms, computation, approximations, indirect analysis, alcoholometry, food preservatives, electrical units and heat and thermo-chemistry.

A very interesting feature of the book is the presentation of several concise descriptions of analytical processes. For example, one section is devoted to the subject of water analysis, another to the cupric oxide reducing powers of the carbohydrates, another to beer analysis, and still another to the estimation of chicory in a mixture of chicory and coffee.

Considerable value is given to the book by the section on oils, fats and waxes, consisting of notes, tables and other data, as well as by the pages devoted to notes on the various indicators. Some space is given to the British regulations governing the sale of butter, margarine and milk, and, as might be expected in a book of this type, the subject of weights and measures is thoroughly taken up by the use of equivalents and methods of transposition.

With its wealth and selection of material this handy little book is bound to become a helpful companion to the laboratory worker and analyst.

E. J. HUGHES.

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TRAVAUX DU LABORATOIRE DE MATIÈRE MÉDICALE DE LA FACULTÉ  
DE PHARMACIE DE PARIS. Vol. xii, 1920.

This work is divided into four parts: Part I comprises a report by Émile Perrot and Ad. Alland on Gum Arabic, Senna, and several other medicinal, edible and industrial products of the Anglo-Egyptian Soudan. The authors include in this splendid article their observations on the vegetation encountered on their trip from Cairo to Kordofan, a note on the principal exportations of vegetable products of the Anglo-Egyptian Soudan and comments on the economic prospects of this region. They have elaborately illustrated it with 44 fig-



ures of plants and scenes encountered on the trip along with a map of the Anglo-Egyptian Soudan.

Part II comprises a doctorate thesis written by François J. Doré, entitled "La Therapeutique et L'Hygiene en China" ("Therapeutics and Hygiene in China"). The author discusses the influence of superstitions in China on the development of the medico-pharmaceutical sciences of that country.

Part III is a treatise on "Composition Chimique du Bacille Tuberculeux" ("Chemical Composition of Bacillus Tuberculosis"), by A. Goris. In this article the author gives the history of the subject and then discusses the methods employed and results attained in his personal investigations. Both the organic and mineral constituents are described and observations recorded on the acid resistance of the organism.

Part IV comprises two articles. The first of these, by Professor Émile Perrot and G. Blaque, is entitled "Les efforts de l'étranger pour la production des drogues vegetales" ("Foreign efforts for the production of vegetable drugs") and treats of the recent work (up to 1920) in this direction in Germany, England, Canada, India, Austria, Belgium, United States, Holland, Dutch East Indies, Hungary, Italy, Poland and Russia. A bibliography of some of the recent literature bearing upon vegetable drug production accompanies the article.

The second article, by A. Goris and Ch. Vischniac, treats of the character and composition of primeverose from *Primula officinalis* Jacquin.

H. W. Y.

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FRENCH-ENGLISH DICTIONARY FOR CHEMISTS. By AUSTIN PATTERSON, PH. D., formerly Editor of "Chemical Abstracts." John Wiley & Sons, Inc., New York, 1921; xvii+384 pages, 5 by 7 inches; \$3.00 postpaid.

This book is a companion volume to the author's "German-English Dictionary for Chemists." As stated in the prospectus, "everything possible has been done to make the reader of chemical

literature independent of any other French dictionary." The book contains over 32,000 entries and covers the entire chemical field, as well as much that is pharmaceutical, medical and botanical. Also, all common general words which are likely to appear in scientific literature are defined. There is included a general statement covering the conjugation of French verbs and a series of notes intended to assist in the use of the vocabulary. In short, the general scheme is such that the book should be available even to those least familiar with the French language. While the book is intended primarily for the translation of French chemical literature, it should prove of service in the translation of pharmaceutical literature as well.

R. R. F.

# THE AMERICAN JOURNAL OF PHARMACY

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## EDITORIAL

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### THE ALCOHOL PROBLEM.

The Prohibition Amendment constitutes one of the most radical modifications of general law that the world has ever experienced. The extinction of slavery was a violent change, but the slave area was a comparatively small part of the United States, and the other great nations had long since abandoned the system and even placed it under active condemnation. The use and abuse of alcoholic beverages go back to the remotest periods of written history. They have been always associated with the joyous side of life, and have also been regarded as valuable therapeutic agents. The Amendment practically cuts out all these relations, for as interpreted by the Act of Congress the proportion of alcohol permissible is so far below that in the normal beverages as to be regarded by the mass of the people as without value.

Undoubtedly this remarkable legislation has been largely due to the persistent refusal of the liquor interests to control in any way the objectionable features of the traffic. Just as the slave-lords, in the first half of the nineteenth century, not only refused to mitigate the cruelties of slave life, but demanded further extension of it and unlimited privileges, so the liquor interests, making no effort to reduce the abuses of the saloon, selling without hesitation to unlicensed places and in many other ways showing an indifference to law and order finally aroused so much opposition that, as in the case of slavery, the whole institution was swept away, without regard to the economic effects or abstract legal principles involved.

In the present state of affairs, the position of the practicing pharmacist is serious. In proportion as law enforcement eliminates the saloon or throws it into alleys and by-ways, the drug store is

liable to become the substitute, and it behooves all who have the maintenance of pharmaceutical ethics at heart to use every effort to counteract this tendency. Black sheep there will be in spite of all teaching and example, but the faculties of our pharmaceutical colleges and the controllers of pharmaceutical organization must preach in and out of season the duties of the retail pharmacists with no uncertain voice. The question is, of course, seriously complicated by the general opinion that alcoholic beverages have a medicinal value, and by a somewhat widespread opinion that they have also a food value. It cannot be denied that moderate amounts of alcohol are consumed in the animal system with production of energy, but it can be easily shown that such energy is more expensive than that from any common article of diet. The view that a moderate amount of alcohol has a so-called "protein-sparing" power never had any satisfactory experimental basis, and does not now form any part of scientific opinion in this field.

A phase of the alcohol question that needs active discussion is that of adulteration. Habits die hard, and those addicted to the use of alcohol, or lenient in regard to its use in others, are found very frequently repeating the shibboleth that if only "pure" liquors would be sold the evils of intoxication would be materially abated. The widespread notion that poisonous substances are frequently added to beverages, especially those sold in violation of law, finds no support in the experiences of chemists. It is true that, lately, a good many cases of adulteration with methanol (or even complete substitution of this substance) have been reported, but such practices lead usually to the just punishment of those who drink the liquor, inasmuch as such admixture is generally found only in liquors sold in violation of the law. The dangerous ingredient in alcoholic beverages is the alcohol; the stories of the use of strychnin in beer and of cocculus berries in other liquors are like the stories of arsenic and opium in cigarettes, sand in sugar or chalk in milk, the invention of newspaper reporters.

The value of alcoholic beverages in treatment of disease is as yet an unsolved problem. It cannot be doubted that a substance that has such prompt and toxic effects as alcohol must have applications in rational therapeutics, but alcohol differs from almost all other remedial agents in the gustatory characters of its commercial forms. If the only available form was the silent spirit, that is, the almost

flavorless mixture of ethyl hydroxide and water, it is probable that alcoholic excess would be much less frequent, although it is true that many persons have such depraved taste that even disagreeable mixtures will be drunk for the sake of the intoxicating effects. It is along the line of this medicinal use that the greatest danger lies, and it is a danger especially affecting the retail druggist, who is constantly and unavoidably brought in contact with those who resort to self-medication. Unless the attitude of the mass of druggists is held in uncompromising antagonism to any deference to those who seek to secure alcoholic beverages under the excuse of illness, there is grave danger that the corrupting influence of the saloon will be transmitted to the drug store, and the latter become an outpost in the underworld.

HENRY LEFFMANN.

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## ORIGINAL PAPERS

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### VISITING OLD FRIENDS.

A BRIEF ACCOUNT OF A SEPTEMBER BOTANIZING TRIP IN SOUTH  
JERSEY.

By CHARLES H. LAWALL, PH. M.

A professor of pharmacy and his assistant, an ex-president of the American Pharmaceutical Association and two ex-presidents of the Philadelphia local branch thereof, a former presiding officer of the Pennsylvania Pharmaceutical Association, the dean of a pharmacy college, a hospital pharmacist and assistant pathologist, an ex-chairman and present member of the U. S. P. Revision Committee, a member of the A. Ph. A. Committee on Druggists' Recipe Book, a member of the National Formulary Revision Committee, an instructor in pharmaceutical arithmetic, two members of the American Chemical Society, a member of the Philadelphia Botanical Club and one of the Pennsylvania Botanical Society—all these fared forth one fine day in early September to renew their acquaintance with the flora of the coastal strip and adjacent mainland in the neighborhood of Great Egg Harbor Bay, New Jersey.



TYPICAL CEDARS ALONG A WIND-SWEPT WASTE.



WATER LILIES.



WHERE TIDES AND MEADOWS MEET.



WILD CARROTS IN AUTUMN.

The conveyance used was a small touring car, of which the whole party occupied the front seat. Impossible? Not at all, for you see, there were only two individuals, after all. In the rear seat and on the floor of the car were piled a vasculum, several cameras, two pairs of rubber boots, a large vase and several handbooks on systematic botany.



SEASIDE GOLDEN ROD.

The sea breeze blowing on their backs had a tang of autumn in it, although the sun was warm overhead. Away across the meadows and marshes were many plants recognizable at a distance. Clumps of bayberry and groundsel here and there relieve the flat monotony of the landscape. On the borders of the woods lining the western side of the coastal strip were rows and thickets of staghorn



and upland sumach, with now and then a sassafras standing out, showing promise of reds and yellows to come when the leaves are frost touched.

The sea rocket sprawled over the level sandy places and the deeper green of patches of beach heather carried the thought back to early summer when the golden, insect-laden blooms vie with the purple of the lupine in catching the eye of the speeding wayfarer along miles of pine barren roads.

The seaside golden rod, almost bush-like in size and growth was seen on every side.

The procumbent sensitive plant with its yellow flowers and irritable leaves bordered the foot paths, while the Indian mallow and clotbur, coarse-leaved and despised by man and beast alike, were everywhere abundant.

The omnipresent bouncing bet, the common pepper grass, the yellow flowered mustard, the yarrow with its delicate fern-like foliage, the smartweed and an occasional daisy, were familiar friends whose absence would probably make them more conspicuous than does their presence, they are so homely and common. In this recital of the commonplace must not be forgotten the diminutive black nightshade everywhere underfoot, nor the ungainly evening primrose, an ugly plant with a pretty name.

In the open spaces of the meadows could be seen the saltworts and samphires, which in October and November flood the scene with a crimson haze as one looks toward the horizon. In among the waving marsh grass were clumps of sea lavender, sometimes called marsh rosemary, which was at one time official in the U. S. P., but which has long since been discarded from medical practice. A bunch of these plants makes a fine winter bouquet.

Each little tidewater thoroughfare is outlined by the tall grasses bordering its course, and the pattern of their lines of deeper green is conspicuous and curiously intricate and attractive, reminding one of a gigantic picture puzzle.

As soon as the mainland is reached other interesting and familiar plants are encountered. The ubiquitous poke and the dreaded poison ivy greet one from almost every fence corner. This selective distribution is ornithological in its etiology. The choke cherry also is frequently found in similar situations for the same reason.

Back of the fences, along the edges of cultivated fields are tangled patches of wild blackberry and dewberry, with wild strawberry plants, now long since the fruiting stage, peeping up between. The wild rose shows by its abundant red hips, the glory of the bloom that has passed with early summer. The beach plum, low and straggling, the haven of nesting birds, is now hung with purple fruits of honied sweetness with an attractively bitter after tang. The Virginia creeper, its older leaves already changing to scarlet, clambers over fence and tree, showing marked contrast to the deep mossy green of the cat brier, which loves the edges of thickets and deep, cool woods.

Leisurely traversing the country by the smaller wood roads, many interesting trees and shrubs are noted. The scrub pine is predominant in certain areas, accompanied by the ubiquitous swamp and blackjack oaks. The foreground is of bracken, with sensitive fern bordering the roads. Against the skyline as we leave the marshes are rows of cedars with their wind-twisted branches, distorted but defiant, exemplifying adaptability and stubbornness at the same time, often assuming grotesque shapes or reminding one of all kinds of unrelated things.

In the roadside thickets on the edges of the woods, the sweet pepper bush reaches out its fragrant white flower clusters. Here and there stands up a button bush with its globular flower heads, as if in martial salute. An occasional glimpse of the glossy, deep green, spiny leaves of the holly remind us of Yuletide decorations and seem strangely out of place. Its closest relative, the black alder, too, with its berries in close-clustered whorls, now beginning to turn red, is a reminder of Christmas wreaths.

Here and there a glimpse of a single scarlet branch on a tree yet robed in living green, calls attention to the two trees that even in midsummer anticipate the brilliancy of their autumn foliage. They are the sour gum with its oval, and the sweet gum with its star-shaped leaves. Dogwoods, huckleberries and blueberries, laurels, both the calico bush and the diminutive sheep laurel, and an occasional viburnum, are observed as we go further inland.

As we pass a marshy woods, the silvery, silky undersides of the swamp magnolia leaves are visible in all directions, and one longs for the fragrance that surrounds the spot in early June, when their tightly wrapped, cream white buds shed a woodsy odor, which often perfumes the air for miles at a stretch. Here we pass a thicket, in the

midst of which the tall and stately Turk's cap lily, having just completed flowering, thrusts its fruit up conspicuously, while along the very edge of the road the day lily, too, is noted in the fruiting stage. Here a rag weed flaunts its hay fever-compelling blooms and there the coarse sow thistle stands up in vulgar arrogance.

The tall wool grass beckons us to take it along for a decoration lasting all the year, while the beggar's ticks and tickseed dare one to venture within their reach.

An old, neglected clearing, once a cultivated field, affords a rich botanical repast. Here is the brilliant bloom of the orange milkweed, almost recumbent, while quite near and much higher are the purple globular flower clusters of the common milkweed, already beginning to shed their silky plumes from earlier borne flowers. Underfoot is the self-heal, while its distant relative, the horse-mint shows in scattered clumps of purplish brown.

The delicate purple *Gerardia* monopolizes the open spaces, while just inside the dry woods, at the edge of the clearing, is seen its yellow-flowered cousin, the downy false foxglove. Along the hedgerow is a purple-flowered spirea, and a patch of tansy and a mulberry tree are evidences of a former habitation, of which the ruins of an old cellar wall give confirmation. Here, too, is blue vervain and scattered about in profusion may be seen black-eyed Susans, wild sunflowers and boneset.

Golden rod and asters are plentiful both as to numbers and variety. One of the conspicuous features of a cleared patch of this sort are the clumps of wild indigo, almost as regular in form as though a landscape gardener had trimmed them, with the blue-green, characteristic foliage which defies all effort at preservation in a herbarium.

Then, too, there are the clovers, the red and white, and sometimes the Alsike, usually seen in isolated patches. The silky soft heads of the rabbit clover, also known as old field clover, from its tendency to spread where cultivation has been abandoned, give a grey mistiness to the vista, on looking across the level stretches, that is peculiarly attractive.

Patches of vetch in riotous exuberance catch the eye and in all directions we can see the lacy blooms of the wild carrot, slightly convex in the early stages, but reversing this form as the flowers pass maturity, the final fruiting clusters looking like a bird's nest on the end of a stem.

Groups of fireweed, ugly and persistent, strike a discordant note now and then which is relieved by its silky gray competitor, life everlasting, so often used for filling fragrant pillows and cushions for tired heads. On one side is a dry woods, where by walking but a few steps from the road is found the three wintergreens, the *Gaultheria* or fragrant, the *Chimaphila* or spotted, and the *Pyrola* or shin-leaf. Here, too, is found the *Mitchella* or teaberry, also called partridge berry, and an occasional rattlesnake plantain, which belongs to the orchid family.

Over to the right is a deeper green and greater luxuriance of foliage which promises much, if, as we hope, it is a cedar water pond or a cranberry bog. On the edge we find iron weed and Joe-pye vying for supremacy. As we approach nearer to the water the lush damp grass, we see, is dotted with many colors of flowers loving wet places. Here we find the deer grass or meadow beauty alongside the blue-eyed grass, neither of them, however, being really grasses. The cross-leaved or marsh milkwort, with its purple flower heads is intermingled with the orange milkwort, sometimes known as the wild bachelor's button. The marsh pink or *Sabbatia* here shows its starry pink flowers with their contrasting yellow centers.

The common lobelia, known as Indian tobacco, is found here and almost at the water's edge we find the wild cranberry plant, with flowers and fruit both present at the same time. Most persons have an idea that cranberries grow on bushes and are surprised when they first become acquainted with the plant as it grows and see its diminutive size as compared with its fruits.

Now we reach an opening that leads to the water's edge and looking across the amber transparency of the cedar pool, dotted with islet-like clumps, we are confronted with a scene of unusual beauty. Along the edge are tall, graceful plants of meadow rue, the beauty of whose finely divided foliage is unmatched by any other plant of its size. The spotted hemlock rises to a height of five or six feet with its umbels of white flowers borne on purple stalks. The button snakeroot or rattlesnake master, with its steel blue flower clusters and feathery foliage is striking in its individuality.

Lower down the cardinal lobelia makes a bright spot of contrast with the deep blue giant lobelia, which accompanies, and the white waxy blossoms of the arrowhead are again contrasted with

the bright blue of the pickerel weed now passing into the chaffy, brown fruiting stage. The white, button-like tops of the pipeworts remind us of a collection of hatpins stuck in the marsh at various angles. The yellow blossoms of the spatter docks look vulgar and common when contrasted with the blooms of the white fragrant water lilies lying outspread in graceful symmetry of both leaf and flower. The sword-like leaves of the several species of iris which had bloomed some time since, are in close resemblance to the foliage of the bulrushes or cat tails which are now approaching maturity.

Back in the swampy edges are clusters of plants of the cotton grass, each stalk looking for all the world like a bunny's tail tied on the end of a stick. At our feet, half submerged, lie the deep blue-green, large velvety leaves of the golden club, which bloomed in early summer. Just at the water's edge is a pitcher plant with its curious, pouch-shaped leaves, and its nodding red and yellow, button-shaped flower. Lower down and only seen when searched for are the sundews, both round and thread-leaved, and the delicate yellow-flowered bladderwort, buoyed up by its balloon-like foliage.

After such a treat we are well content to turn our course homeward, for we have stored in our memories pleasant scenes and have a feeling down in our hearts that we have been close indeed to nature.

"What is the score?" says the professor to his assistant. "One hundred and eleven," is the answer, for copious notes have been taken as we sped along. "Here is another one," shout both the pathologist and the botanist, just as home is reached on the sandy spit, and there, forgotten and overlooked, in the front yard stands a fine specimen of that alien immigrant, long since naturalized, the Jimson weed.

"And here is one for a finale," says the professor as he steps upon a specimen of the sandbur, so appropriately named *cenchrus tribuloides*.

"Are you going to write this up?" asked the instructor in pharmaceutical arithmetic. "If so, which book are you going to follow for the botanical names, Gray or Britton & Brown?" "Forget the botanical names," answered the Dean. "This was purely a pleasure trip, not an educational one."

## DETERMINATION OF CAMPHOR IN CAMPHORATED OILS.

By D. A. WALLACE AND S. B. PLUMMER.

The object of this investigation was to determine the experimental conditions for the correct estimation of camphor, dissolved in cottonseed, olive, peanut and sesame oil, by the methods of, firstly, volatalizing the camphor; secondly, by the use of a saccharimeter with a bichromate cell. These oils were selected as being those specified by the British or United States Pharmacopœia.

The first method consists in heating a known weight of camphorated oil at 120° C. until the camphor has volatalized,<sup>1</sup> the loss in weight, after allowing for the change in weight of the oil, representing the amount of camphor contained in the sample. The time necessary for complete evaporation at this temperature was determined. Likewise an examination of the oils before and after heating, with and without camphor was made, to find what changes in such physical and chemical properties of the oils, as refractive index, iodine absorption and saponification values had taken place. Likewise the change in weight on heating the oils alone was measured.

Japanese camphor was resublimed many times in ordinary desiccators placed on a warm electric plate, until further sublimation failed to change its melting point, the camphor so obtained was used throughout as being sufficiently pure for the purpose.

In Table I are given the physical and chemical constants of the oils employed; the specific gravities were determined by the Westphal balance at 15° C., the refractive indices were determined by both the Zeiss-Butyro and Abbe refractometers at 40° C., the saponification values were made according to Köttestorfer's process and the iodine numbers by Wijs' method. The values recorded are the average of two or more determinations.

TABLE I.

Oil	<i>S. G.</i>	<i>Butyro-Refractometer.</i>	<i>Abbe Refr.</i>	<i>Saponification Valuc.</i>	<i>Iodine Number</i>
Cottonseed . . . .	0.924	57.7	1.4648	198.7	110.4
Peanut . . . . .	0.918	56.3	1.4639	192.8	97.8
Olive . . . . .	0.916	54.0	1.4622	192.7	84.0
Sesame . . . . .	0.923	58.5	1.4652	193.1	104.6

<sup>1</sup> Allen's Comm. Organic Chemistry, Vol. 4, p. 199.

From these determinations all of the oils would appear to be commercially pure, the cottonseed oil gave a high saponification value, whilst the refractive index of the olive oil is slightly below normal.

Standard solutions of camphor were then prepared, eighty grams of the various oils were weighed into glass stoppered bottles and exactly twenty grams of camphor added, giving solutions 20 per cent. by weight, as required by the British and United States Pharmacopœia. After the solutions were uniformly mixed, five gram samples of each were weighed, into five centimeter diameter platinum dishes and placed in a Freas oven, previously regulated to 120° C. At the same time four gram samples of each oil were weighed into similar dishes and heated in the same oven. At the end of two hours all the samples were removed from the oven, desiccated for twenty minutes, and weighed. This process was repeated for a third and fourth hour. The weights at the end of the fourth hour were very little different from those at the end of the third, except in the case of cottonseed oil, which was heated for a fifth hour.

The refractive indices, saponification values and iodine numbers of the oils after being heated both with and without camphor, for five hours in the case of cottonseed, and four hours in the other cases, were then determined, with the following results:

TABLE II.  
REFRACTIVE INDICES (ABBE) AT 40° C.

Oil	Before Heating	Heating	
		with Camphor.	without Camphor
Cottonseed ..	1.4648 (58.3)	1.4680 (63.2)	1.4667 (61.2)
Peanut .....	1.4639 (56.9)	1.4660 (60.2)	1.4654 (59.2)
Olive .....	1.4622 (54.3)	1.4631 (55.7)	1.4626 (55.0)
Sesame .....	1.4652 (58.9)	1.4687 (64.3)	1.4679 (63.1)

The equivalent Butyro refractometer readings are included in brackets. The effect of heating the oils has in every case been to raise quite appreciably the refractive index,<sup>2</sup> a greater effect being produced on the oil when containing dissolved camphor. These values may afford some information for the identification, by means of the refractometer, of these oils after heating to volatilize camphor.

<sup>2</sup> Compare Utz (Chemical Technology & Analysis of Oils, Fats & Waxes, p. 343, V. I).

TABLE III.  
SAPONIFICATION VALUES.

Oil	Before Heating.	Heating with Camphor.	Heating without Camphor.
Cottonseed . . . . .	198.7	198.8	199.0
Peanut . . . . .	192.8	193.7	195.0
Olive . . . . .	192.7	193.3	193.5
Sesame . . . . .	193.1	194.3	194.0

TABLE IV.  
IODINE NUMBERS.

Oil	Before Heating.	Heating with Camphor.	Heating without Camphor.
Cottonseed . . . . .	110.4	97.4	99.05
Peanut . . . . .	97.8	85.5	88.4
Olive . . . . .	84.0	78.5	81.7
Sesame . . . . .	104.6	97.9	99.7

The saponification values were but little affected by prolonged heating, whilst the change produced in the iodine values, due to probable oxidation of the oils would have to be taken into account in utilizing such determinations for the identification of oils after heating to drive off camphor. Tolman and Munson<sup>3</sup> found the iodine value of peanut oil to fall as low as 77 after prolonged heating.

The following table shows the effect produced by heating five grams of the 20 per cent. camphorated oils and four grams of the oils (Blank Oil), for the number of hours indicated in 5 cm. diameter platinum dishes at 120° C.:

TABLE V.

Oil	Hours Heated	Apparent Loss of Camphor.	Blank Oil, Gain Gms.	Blank Oil, Gain %	Cor- rected Loss.	% Camphor Evaporated.
Cottonseed . . . . .	2	0.8885 gms.	0.0065	0.163	0.8950	89.50
	3	0.9743	0.0114	0.285	0.9857	98.57
	4	0.9815	0.0135	0.337	0.9950	99.50
	5	0.9855	0.0142	0.350	0.9997	99.97
Peanut . . . . .	2	0.8830	0.0086	0.215	0.8916	89.16
	3	0.9827	0.0126	0.315	0.9953	99.53
	4	0.9895	0.0138	0.345	1.0033	100.33*
Olive . . . . .	2	0.9875	0.0035	0.0875	0.9910	99.10
	3	0.9897	0.0086	0.215	0.9983	99.83
	4	0.9880	0.0108	0.270	0.9988	99.88
Sesame . . . . .	2	0.9977	0.0006	0.015	0.9983	99.83
	3	1.0017	—0.0010	—0.025	1.0007	100.07*
	4	1.0034	—0.0015	—0.0375	1.0019	100.19*

<sup>3</sup> "Olive Oil and Substitutes," U. S., Bureau of Chemistry Bulletin No. 77, p. 45, note e.



The values indicated by \* are probably accounted for by the oxidation of the oils proceeding faster in presence of camphor than when heated alone. This view is confirmed by the iodine values, above obtained, being smaller for the oils from which camphor had been volatilized than for the oils heated alone for the same length of time; if so, it would follow that the gains recorded under (Blank Oil), representing the increase in weight of the oils due to oxidation on heating the oils alone, are slightly less than should actually be added to the "apparent loss" to give the actual loss.

From these determinations, which have been limited to the examination of one sample of each oil, camphor in camphorated oil may be determined from the loss in weight on heating in platinum dishes at 120° C. for five hours in the case of cottonseed, four hours in the case of peanut and olive, and three hours in the case of sesame oil, after adding 0.35, 0.26, 0.27 and minus 0.042 per cent., respectively, of the four grams of oil taken for the experiments.

## OPTICAL ROTATIONS.

The optical rotations of the camphorated oils were determined by a half-shadow, single wedge compensating saccharimeter, using a nitrogen lamp as source of light. To eliminate, as far as possible, the difference in the colors of the field of view a cell containing two centimeters thickness of 10 per cent. bichromate solution was placed between the light and illuminating lens. An appreciable difference was noted when observations were made at one time with and at other times without the dichromate cell. The reading recorded are the average of several measurements and are for a 200 mm. tube at 20° C.

TABLE VI.

Oil.	Rotation of Oil.	Rotation of Campho- rated Oil	Absolute Rotation.	Angular Rotation.	Angular Rotation for 1% Camphor.
Cottonseed ..	-0.45° V.	56.6° V.	57.05° V.	19.79 ang.	0.989 ang.
Peanut .....	-0.1	56.90	57.00	19.72	0.986
Olive .....	0.2	57.4	57.20	19.82	0.991
Sesame .....	2.85	59.25	56.40	19.56	0.978

From these results the calculated angular rotation for a 200 mm. tube is about 0.98-0.99 for each per cent. of camphor for solutions of standard pharmacopœial strength.



institution—although on April 5, 1821, the University did, indeed, proceed so far as to confer the honorary degree of master of pharmacy upon sixteen apothecaries of Philadelphia, the first grant of a pharmaceutical degree in this country.

The College was founded in historic Carpenter's Hall, a building occupied in 1774 by the Provincial Assembly which recommended a general Congress of all the American Colonies, which Congress also met in this hall, and within it inaugurated those measures which, after the perils of the Revolution, terminated so favorably for civil liberty in America and throughout the world; and so, within this hall the "sixty-eight druggists and apothecaries" met and wrote a new declaration of independence: That pharmaceutical education shall be of pharmacists, by pharmacists and for the public welfare.

Prior to 1821, "in this new country with its sparse population and vast territorial extent—its few small but growing cities scattered along the seaboard—the occasion had scarcely arisen to put into practice the obvious educational means fitted to meet these requirements; but now the time had evidently come. Every intelligent druggist and apothecary felt that the instruction which might be suitable for the student preparing himself for the duties of the physician would be only partially fitted for one who was to assume the widely different responsibilities of the drug store and dispensary." (Historical Memoirs of the Philadelphia College of Pharmacy, Edward Parrish, AMER. JOURN. PHARM., 1869-97.)

Furthermore, the founders of the College realized that their responsibilities were not only to provide pharmaceutical education, but also to protect the public against the adulteration and misbranding of drugs; thus, at the second meeting of the College (March 13, 1821), a committee appointed at the first meeting reported that abuses had crept into the drug and apothecary business; instances had occurred of deteriorated drugs being introduced into the shops and valuable remedies in daily use being adulterated and sold of inferior quality and that such abuses were attributable in part "to want of proper pharmacological information on the part of some druggists and apothecaries who vend and of physicians who buy," and it was recommended, with the establishment of the College, that its "attention be constantly directed to the quality of articles brought into the drug market, subjects relating to the business and its objects be

discussed, and information beneficial and instructive to the trade communicated."

It is of interest to note that "the first years of the College were marked by great activity. Committees of inspection were appointed to examine drugs introduced into the market, and to expose adulteration and sophistication. Latin labels were printed, carefully adapted to the officinal standard of nomenclature. Formulas were published for the old English remedies called 'patent medicines,' then very extensively sold, with a view to greater uniformity in their composition and properties; and the absurdly-worked wrappers in which these were enveloped, giving false or exaggerated accounts of their virtues, were measurably superseded by more sensible and truthful 'directions.' Meanwhile, a library was being formed, a cabinet of the specimens collected, and the various improvements in chemistry and pharmacy suggested from time to time were investigated and reported upon" (Edward Parrish).

In this way the College sought to prevent the manufacture and sale of adulterated or misbranded or deleterious drugs and medicines, thereby anticipating in a sense the enactment of the Federal Food and Drugs Act of nearly one hundred years later, but the influence of the College was wholly educational and moral, and no adequate protection was given to the public until the enactment of the Federal Food and Drugs Act of 1906, one of the most righteous laws ever passed by the United State Congress.

And the work so auspiciously begun by the College one hundred years ago has been continued through the century with ever-increasing vigor and efficiency.

The College has achieved its unusual success as an educational institution because it has been built upon the bed-rock of character. The sixty-eight men who instituted the College were mostly members of the Religious Society of Friends, commonly called Quakers, who believed in the homely virtues of modesty, thrift and wisdom, and love of peace and simple honor, and practiced these; men of plain living and high thinking, men of strong and positive opinions, and men of practicality, thoroughness and love of humanity.

And it was this love of humanity, doubtless, that inspired their love of education. As William Penn, the founder of Pennsylvania, wrote: "Friends consider education as a right and a privilege, to the end that the poor as well as the rich may be instructed in good and commendable learning, which is to be preferred before wealth."

The aim of the Quaker founders of the College—and their influence persists to this day—was to give to the youth of the land the most practical and thorough collegiate pharmaceutical education at the lowest possible cost. The intent was not to build up a money-making institution, but to train men and women in pharmacy, and the original charter contained the provision (later eliminated) that the annual income of the College from all real and personal estate should not exceed five thousand dollars. And who shall say that there is not wisdom and truth in this Quaker philosophy of simplicity and thrift in education; because, it is *not* bricks and mortar that make an educational institution great—it is the brains within the bricks and mortar—the brains of earnest, able and devoted teachers reacting with the brains of youth, eager to learn, to think and to do!

During the first fifty years (1821-71) the instruction of the College was in materia medica, pharmacy and chemistry, and in the last four years of that period, in botany, also; and it was wholly didactic.

In 1846 an epoch-making advance was made, when pharmacy was recognized as a distinct branch by the establishment of the chair of theory and practice of pharmacy, and the chair of pharmaceutical and general chemistry was changed to chemistry. In 1867, the chair of materia medica was changed to materia medica and botany, and field work in botany was begun.

During the past fifty years (1871-1921) many additions to the curriculum have been made, such as analytical chemistry, practical or operative pharmacy, pharmaceutical chemistry, commercial pharmacy, pharmaceutical jurisprudence, chemical control in manufacturing pharmacy, scientific research, bacteriology and hygiene, Latin and pharmaceutical arithmetic, as well as special courses in technical chemistry, applied bacteriology, technical microscopy, physiologic assaying, clinical chemistry, advanced pharmacognosy, and perfumery, and the post-graduate courses leading to the degrees of bachelor of science in pharmacy, chemistry, pharmacognosy and bacteriology.

In 1897, the chair of materia medica and botany was divided into materia medica, including physiology, and into botany, including pharmacognosy.

In 1868, when the College moved to its present site, it had three instructors; today it has twenty-three, then 146 students, to-

day more than 600; then, no women students, today fifty; then, no laboratories, today six; then, no post-graduate courses, now four leading to degrees.

In 1920, in order to expand its courses of instruction, the charter was amended and the title changed to the Philadelphia College of Pharmacy and Science.

It is impossible at this time to more than briefly mention the teachers of the past, but during the first twenty-five years those who deserve especial mention are Samuel Jackson, George B. Wood, Joseph Carson and Franklin Bache, all of whom exercised potential influence during this formative period of American Pharmacy.

During the next fifty years the list embraced such widely known authorities in pharmacy as Robert Bridges (1842-79) whose lovable character and long years of unselfish devotion to the College has enshrined him in the hearts of all; Edward Parrish (1864-72), an exceedingly able and inspirational teacher, and the author of the first distinctively American textbook on the practice of pharmacy; John Michael Maisch (1866-93), whose constructive work for the upbuilding of pharmaceutical botany, materia medica and plant-chemistry will last as long as the name of pharmacy endures; and William Procter, Jr. (1846-66, 1872-74), whose researches in pharmacy gave a wonderful impetus to the growth and development of American pharmacy, made it known the world over, and won for himself the name of "The Father of American Pharmacy."

And William Procter, Jr., was succeeded by one who lived in our own time—"the noblest Roman of them all," one who as pharmacist, teacher, educator, author and executive—especially as the Chairman of the Committee on Revision of the U. S. Pharmacopœia for two successive decades—was the outstanding figure of American pharmacy in his day, the teacher of teachers, and the genial warm-hearted, inspiring friend of us all—Joseph Price Remington (1874-1918). "And we ne'er shall look upon his like again."

And then there was one who stood next to Remington, who was most largely instrumental in making the course of commercial training of the College (established in 1899), the first of its kind in the country, so successful, who became one of the foremost figures in American industrial pharmacy, and who loved his Alma Mater and never forgot her, even unto death—Frank Gibbs Ryan.

Motives of delicacy preclude my saying much of those who are

still living, honored representatives who have done yeoman service in the upbuilding of our institution, but the present sketch would be most incomplete did I not refer to one who has borne the heat and burden of the day for the past forty-three years as a teacher in our institution, one who has won national and international renown as a master-mind in pharmaceutical and industrial chemistry—our own, our honored, and our loved Samuel Philip Sadtler.

Quizzing was early instituted at the College and was conducted first by the professors themselves, and in the last 70's, by quiz-masters approved by the Committee on Instruction. In 1880, quizzes were authorized by the Alumni Association, and this constitutes the cornerstone of the present system of quizzing reviews. Later (1886) these were combined with the College reviews and made compulsory (1895), the College assuming full charge.

In 1821, the conditions of the practice of pharmacy were primitive. As Edward Parrish (*AMERICAN JOURNAL OF PHARMACY*, 1871, 481) stated, in 1871, in an introductory lecture to the fiftieth course of the Philadelphia College of Pharmacy:

"Fifty years ago when the College was established, almost every considerable drug store had something like a laboratory attached, where some of the few chemicals then in use and all the galenical preparations were made, and where nearly all the crude drugs were assorted, garbled and packed. The apprentices then enjoyed a wholesome development of muscle through wielding the ponderous pestle, handling the sieves and working the screw-press. He learned how to make pills by the wholesale, to prepare great jars of extracts and cerates, to bottle castor oil, Turlington's Balsam and opodeldoc by the gross, and what he lacked in the number and variety of articles he dealt in, was made up by a greater extent of his operations and the completeness with which, in a single establishment, all the then-known processes were practiced. Very many physicians then dispensed their own prescriptions, drawing the supplies from the druggists, but gradually the separate prescription counter was added to the drug stores, and the dispensing stores, as we now call them, became numerous, and the wholesale druggists gradually ceased to supply the public directly."

Our Quaker forbears realized that pharmacy was both an art and a science, and to be a master of the craft the pharmaceutical student must have practical instruction as well as theoretical, and from the first they required that the candidate for graduation from the College shall have a "practical experience of at least four years

with a person or persons engaged in and qualified to conduct the drug business." Thus vocational training was first established in pharmacy as a prerequisite for graduation.

About the time of the Civil War, a radical change took place in the retail drug business. The manufacturing of drugs and chemicals was taken over by manufacturing houses, more and more, the old apprenticeship custom of legally indenturing youths to learn "the drug and apothecary business" rapidly fell into disuse and the character of practical experience in the retail drug store changed, becoming less and less adequate, so far as manufacturing was concerned; although the underlying principle of drug store experience, with its familiarity with work-a-day technique, continued fundamentally sound. Hence, it became evident, that the College should give laboratory instruction; but the means of the College were limited, and it could not see its way clear, at this time, to give such instruction, especially as it was contemplating the erection of new buildings in the near future.

Next to its teachers, the biggest asset of a College is its alumni, directly and indirectly—directly in exemplifying its teaching and indirectly by its work for the Alma Mater; and no college in any land has more earnest, loyal and enthusiastic alumni than has the Philadelphia College of Pharmacy, including those of the Medico Chirurgical College merged with our College in 1916, and who, in season and out of season, are voicing their praises of its work and worth; and that their words are not idle words, is shown by the fact that probably 85 per cent. of the matriculants of the College come through the influence of its alumni.

As Richard M. Shoemaker, fifty-nine years a graduate of this College and the first treasurer of the Alumni Association (1864), and beloved by all, writes me: "The Alumni Association of the College always has been and is the backbone of all the energies for the advancement of the institution."

And we cannot mention the Alumni Association without mentioning Edward C. Jones, '64, who with his classmate, Albert E. Ebert, '64, founded the Alumni Association, and worked indefatigably for the College and its students. The vessel of clay that held his soul may have failed perhaps to reflect its beauty, but his personality had a charm that endeared him to all; and the good he did lives after him.



And then there was Thomas S. Wiegand (1825-1909) typical of the old school Philadelphia druggist of the last century, who sought by precept and practice to establish pharmacy in this country on a scientific and professional basis; he was elected President of the Alumni Association in 1865, and re-elected for six consecutive terms, and was Actuary of the College for twenty-two years (1887-1909), and as the "Students' Friend" was ever "their very present help in time of trouble." Many of the alumni will recall how much they owe to the wise counsel of that dear spirit of college days whom they lovingly and with all respect called "Uncle Tommy."

In 1864, the Alumni Association began a movement for the raising of funds for the equipment of a chemical and pharmaceutical laboratory; by 1867 the subscriptions had amounted to nearly \$5000, and in 1870 it established a laboratory for instruction in practical chemistry and pharmacy in charge of Prof. John M. Maisch, the first of its kind in America. In 1872 the laboratory was turned over to the College by the Alumni Association. In 1876 its two divisions of work were partially segregated, Prof. Remington giving a course in pharmaceutical manipulations, and in 1878 he assumed full charge of the pharmaceutical laboratory (or laboratory of operative pharmacy), while Prof. Maisch confined his instruction to the chemical laboratory. In 1903 an optional course in dispensing was inaugurated, and the following year it became a part of the regular course.

In the chemical laboratory, Prof. Maisch was succeeded as director by Frederick Belding Power (1881-83), whose famous research work, later, in phytochemistry in the Wellcome Research Laboratory of London is known to you all, and he by Henry Trimble (1883-98), whose research work on the tannins is classic.

The microscopical laboratory was originated also by the Alumni Association, commencing with 1882-83, the Association controlling the instruction in this department until 1894, when the College assumed charge of it as the botanical and microscopical laboratory.

In 1899 optional laboratory courses were established in bacteriology, the study of powdered foods and drugs, fungi and fungous diseases, morphology and physiology, and systematic botany, and in 1913 bacteriological laboratory work became a part of the regular course.

With the enactment of the Federal Food and Drugs Act of

1906, it became apparent that skilled food and drug technicians would be necessary to ensure the proper enforcement of the law, and in 1907 the College secured, largely through the personal solicitations of the late Mahlon N. Kline and Joseph P. Remington, contributions of some thousands of dollars with which it was enabled to erect a food and drug laboratory building and inaugurate a course in food and drug analysis.

Equal in importance to pharmaceutical education is pharmaceutical research, because pharmaceutical practice is, in effect, applied education, and education is applied research; and upon the bases of research, education and practice rest the science and art of pharmacy.

Our Quaker forbears recognized the vital importance of systematized research and in 1821-29 published irregularly a journal devoted to research under the name of the *Journal of the Philadelphia College of Pharmacy*. Beginning with April, 1829, the Journal was issued at regular stated periods, and in April, 1835, the title was changed to the AMERICAN JOURNAL OF PHARMACY. It is not only the earliest periodical of its kind in the world, but it is recognized, at home and abroad, as the leading scientific pharmaceutical periodical of this country.

During the past century, the JOURNAL has published 50,000 reading pages, the larger part of which has been research work in pharmacy, chemistry, pharmacognosy and science. (Note, please, the significance of the initials of these—P. C. P. and S.!) by the faculty and members and contributors to the JOURNAL. Thus, John Farr, of Farr and Kunzi (later Powers and Weightman), in a paper read before the Philadelphia College of Pharmacy, of which he was a member, at a meeting held December 27, 1825, on the subject of "Extract of Quinine" (Proceedings of the Philadelphia College of Pharmacy—later the AMERICAN JOURNAL OF PHARMACY, Vol. I, No. 2, 43), made the following statement: "In the summer and autumn of 1823, a season peculiarly memorable to Philadelphians by reason of the alarming prevalence of intermittent and other fevers, sulphate of quinine was first successfully prepared here," three years after its discovery by Pelletier and Coventou; and it should be stated, also, that Zeitler and Rosengarten (predecessors of Rosengarten and Sons), likewise made quinine sulphate in 1823, their first sale being in December of that year. And it may be added, that "morphine

sulphate and morphine acetate were first manufactured (in this country) by George D. Rosengarten in 1832; and the mercurials and strychnine sulphate in 1834" (Rosengarten and Sons, by William McIntyre, AMERICAN JOURNAL OF PHARMACY, 1904, 303). All of which activities were doubtless inspired by the spirit of original research developed by the College. And William Procter's discovery of the properties of the salicylates (1842) led to the manufacture of synthetic oil of wintergreen and the salicylates. Thomas J. Husband first developed (1837) the manufacture of heavy magnesia in this country. Robert Shoemaker first made (1848) glycerin commercially. Charles Shivers first developed the manufacture of adhesive plaster, making enormous quantities for the Government during the Civil War. William R. Warner first made (1857) sugar-coated pills. Alfred Mellor and Henry N. Rittenhouse first developed the manufacture of licorice extract. And C. Lewis Diehl and William Procter, Jr., first made the process of percolation commercially practicable.

The most important discovery of the Twentieth Century—as important as that of morphine, strychnine and quinine one hundred years ago—was that of diphtheria antitoxin by Behring in collaboration with Kitasato and Wernicke in 1890 and 1892. This discovery reduced the mortality of diphtheria from 40 per cent. to less than 10 per cent. and saved millions of lives. Tetanus antitoxin was discovered by Behring and Kitasato in 1892. During the World War its value as a life-saver was amply demonstrated. Ten per cent. of the wounded on the battlefields of France were attacked by the tetanus bacillus and 90 per cent. of these died of lockjaw. The call came for tetanus antitoxin and millions of doses were supplied to the armies of the Allies, resulting in the control of the deadly infection. These discoveries were speedily followed by others of equal value as life-savers. Typhoid fever, which hitherto had killed more soldiers than the bullets of the enemy was banished from the armies by anti-typhoid vaccination.

It is a matter of pride to us that these wonderful discoveries have largely been made available by our fellow alumni-graduates of the Philadelphia College of Pharmacy, as the H. K. Mulford Company, the earliest and largest producers of biologic products in this country, and who so promptly and successfully met, by means of an immense reserve stock, the call of the allied armies for such products during the World War.

And in the laboratories of the College many workers have solved many problems that have found important industrial applications, while from the faculty and alumni have come original papers of great practical value to medical and pharmaceutical science.

In this work the library of the College with its 20,000 volumes constituting the largest and most valuable pharmaceutical library in the United States, has been found to be of incalculable service; and next in importance has been its museum and herbarium with its many thousands of medicinal plants, its rare and typical exhibits of crude drugs, its raw materials, and its manufactured drugs from all parts of the world.

In the literature of pharmacy and allied science, the College has always been most actively represented, its faculty having issued nearly 200 volumes. Thus, the *U. S. Dispensatory* was founded in 1833 by George B. Wood and Franklin Bache, both of the faculty; John M. Maisch (with Alfred Stille, M. D.) founded the *National Standard Dispensatory* in 1879; Robert Bridges was the American editor of Fownes' *Chemistry* (1845-78), and of Graham's *Elements of Chemistry* (1852); William Procter, Jr., was the American editor of Mohr and Redwood's *Pharmacy* (1849); Edward Parrish wrote his first *Pharmacy* in 1855; Joseph P. Remington's textbook on *Pharmacy* has been the standard textbook on pharmacy since 1885, in this country and many foreign lands; John M. Maisch published in 1881 the first textbook on *Materia Medica* in this country; Henry Kraemer wrote his first *Applied and Economic Botany and Pharmacognosy* while at the College (1897-1917); Henry Trimble published his *Tannins*; Frank X. Moerk issued his *Qualitative Chemical Analysis*; Samuel P. Sadtler (with Virgil Coblentz) published his *Pharmaceutical and Medical Chemistry*, and his own *Industrial Chemistry*; Heber W. Youngken issued his *Pharmaceutical Botany and Pharmacognosy*; John A. Roddy issued his *Medical Bacteriology*, and Paul S. Pittenger published his *Biochemic Drug Assay Methods*; and with these should be included Julius W. Sturmer's admirable *Pharmaceutical Latin* and *Pharmaceutical Arithmetic*, as he has been affiliated with the College since the Chi-merger of 1916. And there were many formularies and other textbooks published that are not now in general use.

Prior to the U. S. Pharmacopœial Convention of 1850, pharmacists had no active part in the revision of the U. S. Pharmacopœia,

the work being done by medical men. But at the 1840 Convention the Philadelphia College of Pharmacy presented for consideration "a complete revised copy of the Pharmacopœia elaborated with ability and great industry, and the Committee accepted after deliberate examination, nearly all the suggestions" (U. S. P. IX, X); and thus was paved the way, logically, for the representation of pharmacists in all subsequent revisions, and in all of these the College has been most ably represented. Twelve of the thirty-three present pharmaceutical members of the Committee of Revision are P. C. P. men, and the last three Revision Committee chairman—Remington, LaWall and Cook—have been (or are) members of the faculty of the College.

The American Pharmaceutical Association, which stands for the highest ideals of pharmaceutical practice, and is the backbone of professional pharmacy in this country, was organized in the Philadelphia College of Pharmacy in 1852, its first president being Daniel B. Smith, the then president of the College; and from the time of its organization, the members and graduates of the College have been so active in its work, occupying many important official positions, and in the various State and local pharmaceutical associations, in the State Boards of Pharmacy, and as teachers in many schools of pharmacy, that the College has often been referred to as the "The Mother School of American Pharmacy."

What of the future? The past is yesterday and the future is tomorrow! We have been given a glorious heritage and must maintain the traditions of the fathers and justify their faith in us. How can this best be done? It seems to me that five things, chiefly, are essential: (1) Better education, (2) better legislation, (3) better practice, (4) better relations with the medical profession, and (5) better research work.

We must have better education, that is, higher entrance requirements, better facilities for instruction, including a drug plant garden, and better courses of instruction. Beginning with 1923-24, the College will require high school graduation, or its equivalent, for entrance, and we are now working for better facilities and advanced instruction.

And it may be possible for the College to give a pre-medical course for medical students provided such course is organized on a scholastic basis and approved by the Association of American



We must have better research work, because research is the life-blood of education and practice. As Dean Charles H. LaWall writes me, "The future development of pharmacy is largely dependant upon the stimulation of research, especially its inculcation in the student-body. The work of the College in the past has been of the highest character, but it has been done unsystematically, and was largely a matter of chance that it was done at all. Men like Maisch, Procter, Remington, Sadtler, Kraemer and others have simply bubbled-over with initiative, and their efforts have enriched pharmacy and made it better. Today, however, the output is limited, because every member of the faculty is driven full-speed in taking care of his teaching and accessory work. To overcome such a handicap, the teachers should have more assistants for instructional work. The progress of any department of the College could then be measured not only by its instructional results, but also by the quality and quantity of original work it turns out, and the College would have a standing among other scientific schools that instruction alone could not give. Furthermore, students, graduates, members of the College, and others, would be inspired to follow the example of the faculty, and the field of research would be developed and co-ordinated." And as if in anticipation of such a possibility, the Board of Trustees of the College has recently established a sub-committee on research of its Committee on Education to systematically promote research work in pharmacy and correlated science.

And the field of research is practically unlimited. As John Uri Lloyd, a Master in Pharmacy of this College (1897), and one whose research work in pharmacy for the past fifty years stands out like a beacon-light at home and abroad, writes me: "In my opinion, the field of research is as yet scarcely invaded. Whoever enters it should, with each subject, as a foundation, have his feet on the work others have accomplished, then with open mind, raise his eyes to the blue sky above. He should start with a hypothesis gained from study or experience with related products, and yet expect to fail in whatever thought had speculatively advanced. Disappointment brings then no pain. He should be so bold as to question orthodox theoretical rules and formulæ, and in the face of 'authority' create images and plans of procedure of his own. And yet he should be so timid as to shrink from personal criticism of others, realizing that his own self will rise before him as perhaps the one most subject to criticism un-

der the backward glance. If concerned in the exactions of science, he should expect resistance from those whose idols he touches with even the kindest intent. If conscious of the correctness of his views he should make no retort; *time* will care for *fact*. If he has indiscreetly voiced false theories based on fallacious judgment, he should thank the man of the present for service rendered in his disillusionment, resting assured that *time* would later have served the same purpose. If given a moderate period of life the backward glance will surely show a pathway littered with his own broken vases, shattered into fragments by himself. The great charm of research may be defined as the construction of new edifices out of those demolished, and in plant research, the defining and describing of natural textures and plant structures. In this the doors to be opened by the systematically trained scientists of the near future will surely make the life-wanderings of empiricists, with whom this writer is to be classed, pioneer offerings serviceable perhaps mainly as an inspiration to those to follow."

What will the next one hundred years bring our Alma Mater? No man knoweth; time only can tell. And yet paraphrasing Longfellow, let us make our Alma Mater our Ship of State, so strong and great and cry to her: "Sail on! Our hearts, our hopes, our prayers, our tears; our faith triumphant o'er our fears, are all with thee—are all with thee!"

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## SALICIN CONTENT OF BRITISH COLUMBIAN WILLOWS AND POPLARS.

By R. H. CLARK AND K. B. GILLIE.

These determinations on the salicin content of various species of willow and poplar native to the Province of British Columbia are the first of a series of investigations on the possibility of economically cultivating within the Province several species of both native and introduced essential-oil and drug-yielding plants.

For many years the Provincial Botanist, Professor John Davidson, has had numerous inquiries, from wholesale drug manufacturers and others, asking advice on the cultivation and collection of medicinal plants. To secure the necessary information experiments are being carried out on a number of well-known drug plants with



a view to ascertaining the relation between the soil and climate of the Province and the percentage of drug produced by the plant, and also to experiment on the effect of various fertilizers in relation to the size of the crop and percentage of drug. Among the subjects to be investigated in the near future are: *Cascara sagrada* from *Rhamnus Purshiana*, atropine from *Atropa Belladonna*, stramonium from *Datura Stramonium*, aconite from *Aconitum napellus*, digitalis from *Digitalis purpurea*, oil of spearmint, oil of peppermint and oil of *Monarda Fistulosa*. These investigations will be carried on jointly by the Departments of Botany and Chemistry.

There are several reasons why such an industry might thrive within the Province; we have a large number of plants indigenous to the Province which are known to yield oils and other drugs of economic value; we have climates and soils of so varied a nature that it is possible to find localities suited to the cultivation of such plants; there is a large demand for soap, pomades and similar perfumed products in the Oriental markets, easily accessible from the western coast. There is no doubt that many of the plants adapted to a temperate climate could be grown somewhere within the Province. The chief questions arise in connection with a precise choice of locality and the cost of production, and this again would depend on the cost of cultivation and also on the quality and quantity of the drugs which could be obtained. Such questions can only be answered by experiment.

#### SALICIN.

Salicin [ortho-hydroxy-benzyl-glucoside,  $C_6H_4(OC_6H_{11}O_5)-CH_2(OH)$ ], was one of the first natural glucosides to be discovered. It occurs in most, but not all, species of willow and poplar bark. It is hydrolysed by mineral acids and by emulsin of almonds, to dextrose and o-hydroxy-benzyl alcohol. As determined by this enzyme action, salicin must be a glucoside.<sup>1</sup> Populin, another glucoside, also occurs in the leaves and bark of poplars. It is not, however, hydrolysed by emulsin of almonds.<sup>2</sup> On the other hand, it may be hydrolysed by barium hydrate to benzoic acid and salicin. Salinigrin, a third glucoside, has been found in only one species of willow, *Salix discolor*.<sup>3</sup> Helicin, a glucoside isomeric with salicin does not occur naturally.

<sup>1</sup> Fischer, Zeit. Physiol. Chem., 26, 61, 1898.

<sup>2</sup> Allen's Comm. Organic Analysis, vol. 7, p. 100.

<sup>3</sup> Jowett & Potter, Trans. Chem. Soc., 77, 707, 1900.

The bark from the following species, *Salix Nuttallii*, *Salix Hookeriana*, *Salix sitchensis*, *Salix lasiandra*, *Salix purpurea*, *Populus trichocarpa* and *Populus tremuloides*, were analysed. We wish to thank Professor John Davidson for his kindness in providing the various samples.

#### METHOD OF ANALYSIS.

The bark was dried for forty-eight hours at a temperature of about 110 degrees. Two samples of each, weighing twenty grams, were taken, and digested separately for three hours with boiling water and the solution filtered. Two grams of lead acetate were then added to the filtrate to precipitate the proteins, which were removed by filtration. The excess of lead was then precipitated by the addition of the required amount of sulphuric acid, and the liquid filtered. To this filtrate was added 100 cc. of the emulsin of almonds solution and the mixture allowed to stand sixty hours, at which time the solution was diluted to two litres and two portions of 100 cc. were taken for analysis with Fehling's solution. The weight of glucose present being found by reference to Munson and Walker's tables.<sup>4</sup> One mole of salicin gives on hydrolysis one mole of glucose.

The emulsin of almonds solution<sup>5</sup> was prepared from sweet almonds, from which the oil had been pressed, as follows: The press cake was macerated for twenty-four hours with water, to which a small amount of chloroform was added. The mixture was then strained through a cloth and two drops of acetic acid were added per 100 cc. of the liquid for the precipitation and removal of the proteins. To the filtrate was then added an equal volume of alcohol, 50 cc. at a time, which caused the enzyme to come down as a fine precipitate, which was filtered off, washed with alcohol and immediately re-dissolved in water, to which a small amount of toluene had been added. The solution of emulsin of almonds so obtained was tested by treating solutions containing known amounts of pure salicin. It was found that the hydrolysis was complete after sixty hours. The results obtained were correct to within less than 1 per cent.

As is seen from the following table of determinations the duplicate analyses are in close agreement, whilst the salicin content of the various species of willow and poplar show a considerable variation.

<sup>4</sup> "Food Inspection and Analysis," Leach.

<sup>5</sup> Allen's Comm. Organic Analysis, vol. 8, p. 6.

Likewise the spring samples in most cases run higher than the corresponding fall samples, in the cases of *Salix Hookeriana* and *Salix sitchensis* a most notable difference was found.

TABLE OF ANALYSES.

<i>Species</i>	FALL SAMPLES.			SPRING SAMPLES.		
	(1)	(2)	<i>Av'g.</i>	(1)	(2)	<i>Av'g.</i>
<i>Salix Nuttallii</i> .....	3.88%	3.92%	3.90%			
<i>Salix Hookeriana</i> .....	0.70	0.84	0.81	4.47%	4.51%	4.49%
<i>Salix sitchensis</i> .....	2.68	2.92	2.80	5.18	5.00	5.09
<i>Salix lasiandra</i> .....	2.45	2.55	2.50	7.32	7.43	7.38
<i>Salix purpurea</i> * .....	....	....	....	2.50	2.53	2.51
<i>Populus trichocarpa</i> ....	0.95	0.96	0.955	3.78	3.88	3.83
<i>Populus tremuloides</i> ....	3.80	3.74	3.77	3.83	3.89	3.86
				2.42	2.48	2.45

It might be pointed out that there is a large quantity of bark at present annually available at the Vancouver basket factory. In addition there is a very large supply of native willow on the lower mainland of the Province and on Vancouver Island.

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## THE ORGANO-METALLIC BODIES.

By HENRY LEFFMANN, M. D.

Of the many classes of organic compounds those in which metallic elements are joined directly to nitrogen or carbon are probably the furthest removed from the what was in earlier days considered specific features of organic substances. Being all synthetic products, they have been very largely studied as matters of pure science, but of late years a practical interest has attached to some of them, and research has received an additional spur.

The first production of an organo-metallic compound seems to have been due to a (probably random) experiment in 1760, when Louis Claude Cadet de Gassicourt, a military apothecary in Paris, distilled a mixture of arsenic oxide and potassium acetate, and

\*Cultivated variety imported from Japan and planted on LuLu Island for basket-making trade.

obtained a liquid fuming in the air and capable of spontaneous combustion. The nature of this long remained unknown, and it was merely designated as "*Cadet's Fuming Liquor.*" A radicle termed "kakodyl" As (CH<sub>3</sub>)<sub>2</sub>, is the basis of the principal ingredients in the mixture, and in 1842 Bunsen by a series of most interesting and wonderful researches, elucidated the chemistry of the subject and showed that the kakodyl radicle can form a large number of compounds, most of which are highly poisonous. One striking exception to this quality was noted in the case of kakodylic acid, HAs (CH<sub>3</sub>)<sub>2</sub>O<sub>2</sub>, the toxicity of which was found to be much less than the content of As would indicate. The investigation of such compounds involves much risk, and Bunsen lost an eye in consequence of the explosion of a tube in which he was distilling one of the compounds. Kakodylic acid was introduced in medical use, but has not found any important applications, and all these arsenicals have given way to the benzene derivatives of which arspheamin is the best known.

The question of susceptibility to ionization is one which must be taken into account in judging of the physiologic effect of any substance, and in the case of poisonous metal, the position of it in the ion will also determine largely its effects. The contrast between the cyanides and the ferrocyanides exemplifies this fact.

The chemistry of the organic compounds of arsenic and antimony has been extensively treated by Gilbert T. Morgan in a work issued a few years ago and a glance at this will show the extent of the researches along this line and the variety and complexity of the compounds already known. It is well known that the original name of arspheamin, "606," was provisionally given because it was the 606th. derivative that was prepared in the effort to find an arsenical that should have a much higher germicidal action than general toxicity, so as to permit it to be used in rather large doses in the annihilation of the specific germ of syphilis. The investigations along this line have continued and today derivatives analogous to arspheamin have been produced in great number, among which are some that appear to be better adapted to therapeutic use than the original compound.

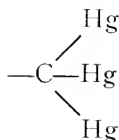
The analogy between arsenic, antimony, nitrogen and phosphorus renders it possible to obtain from the former two compounds of the same type as ammonia and phosphin. These, as might be

expected, show high poisonous properties, and have had no important applications except as asphyxiating gases in war.

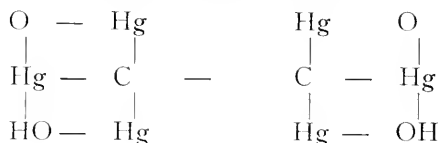
Mercury yields a large number of organo-metallic compounds. The literature of this phase of the subject is extensive, but until recently has not been collected in convenient form, as has been that relating to arsenic and antimony. The enterprise of the American Chemical Society has made available a comprehensive collection of the data concerning organo-mercury compounds, in a volume prepared by Dr. F. C. Whitmore of the Northwestern University, just published. As in the case of the arsenic compounds, the history begins with a somewhat random experiment. In 1843, A. W. Hofmann distilled a mixture of aniline and mercuric chloride and obtained a compound containing mercury in union with a hydrocarbon group, but apparently the exact structural formula of this has not yet been ascertained. In 1850, Frankland noted that metallic mercury acts on ethyl iodide, later found that methyl iodide is changed by the same metal into a methyl mercury iodide,  $\text{CH}_3\text{HgI}$ , and that a similar compound can be obtained from the ethyl radicle. A tragic incident occurred in connection with the early work on these substances, for two of the assistants, Dr. Ulrich and Dr. Sloper, who were working in the laboratory of St. Bartholomew's Hospital, London, where the research was being carried out, were fatally poisoned. Another London chemist accused Dr. Frankland of sacrificing his assistants by imposing on them this dangerous work instead of doing it himself, and for several months the columns of the *Chemical News* were hot with the exchange of correspondence. It appears, however, that no blame can attach to the chief. The methyl and ethyl compounds are liquids of high density, strongly refracting and dispersive, and it was thought that they might be available for filling hollow prisms, but their high poisonous qualities constitute a serious interference.

Interest in the study of organic mercury compounds has been much increased for the same reason that the arsenic compounds have acquired prominence, the use of mercury in syphilis. The need has especially been for non-ionizing compounds which may be used in association with the arsenicals. Just about the time that Frankland obtained the above-mentioned compounds, Sobrero and Selmi discovered another type. By heating mercuric chloride and potassium hydroxide in alcoholic solution, they obtained a yellow slightly ex-

plosive substance containing mercury and carbon, but many others attempted without success to confirm their result. Later, K. A. Hofmann obtained a series termed the "mercarbides" containing the



Some notion of the complexity possible in these substances is shown in the formula of ethane hexamercarbide



A different arrangement results when sodium amalgam is used with the organic bromide and iodides. Both bonds of the diad mercury are attached to the carbon. These reactions, however, so far have been obtained only in the presence of an ester such as methyl or ethyl acetate, which acts as a catalyst, inasmuch as it can be recovered unchanged at the end of the reaction.

Out of the immense mass of compounds of these types a limited number—about two score—are already in the market under copyrighted titles and recommended for medicinal purposes. Some of them contain both mercury and arsenic. How many of them will stand the test of scientific experience it is impossible to say, but all therapeutic history goes to show that ingenious advertising is often the main cause of the popularity of a synthetic drug. However, the scientific features of the organo-metallic compounds will always have a fascination for the chemist.

## MUIRA-PUAMA.\*

BY HEBER W. YOUNGKEN, Ph.D.

This drug, concerning which comparatively little has been written, has been employed in Brazil and France in the form of fluidextract and other preparations for the treatment of various nervous disorders. In recent years it has been shipped from Para and Rio de Janeiro, Brazil, to manufacturing pharmaceutical houses in the United States, where it is made into a fluidextract, which is then sent back to Brazil, there being no particular demand for it here.

The writer, being interested in the botanical source and anatomy of this new article, procured a good-sized sample from one of Philadelphia's manufacturing pharmaceutical houses. This was compared both as to physical and microscopical features with two samples of a root also labeled "Muira-puama," in the crude drug collections of the Philadelphia College of Pharmacy and Science. The three specimens revealed a similar structure and so were undoubtedly of the same botanical source. On the label of one of the specimen jars containing the root appeared the botanical origin, "*Liriosma ovata* Miers."

### DESCRIPTION OF PLANT.

*Liriosma ovata* Miers<sup>1</sup> is a small tree indigenous to Brazil and belongs to the Olive family. Its leaves are short, petiolate, glabrous, up to three inches long and two inches broad, broadly ovate, attenuated at the summit, slightly reflexed along the margin; upper surface light green, lower surface dark brown; venation pinnate-reticulate, more conspicuous on the upper than the lower surface; midrib pubescent above, smooth below. Its inflorescences consist of short axillary racemes, each of four to six flowers.

### DESCRIPTION OF ROOT.

Conical, nearly straight, tapering to a small point, from one-half to one and one-half feet in length and from one-eighth to one and one-half inches in diameter; externally light-brown to grayish-brown, faintly longitudinally striated and beset with short sharp projections, which occasionally unite two or more roots; fracture strongly tough and fibrous; internally light-brown exhibiting a thin bark and broad wood; odor faint; taste slightly saline and acrid.

\*Presented at the annual meeting of the Pennsylvania Pharmaceutical Association, Philadelphia Pa., June 10, 1921.

## HISTOLOGY OF ROOT.

Sections of the root disclose the following microscopical characteristics, passing from periphery toward the centre :

1. Cork, composed of several layers of tabular cells with brownish contents and more or less lignified walls.

2. Phellogen, of clear meristematic cells.

3. Secondary Cortex, composed of a number of layers of parenchyma, some of the cells of which contain a reddish-brown resin, others starch, still others monoclinic prisms of calcium oxalate.

Imbedded in this region are scattered islands of sclerenchyma, accompanied by crystal fibers, the individual cells of which contain rhombohedral crystals of calcium oxalate.

4. Phloem, a narrow zone of sieve tubes and phloem parenchyma. Isolated groups of thick walled bast fibers accompanied by crystal fibers are found amongst the other phloem elements.

5. Cambium, a prominent zone of meristematic cells.

6. Xylem, a very broad central zone of radially arranged wood wedges separated by starch containing medullary-rays. Each xylem wedge is composed of numerous wood fibers with thick, lignified walls, scattered amongst which are starch and crystal containing wood parenchyma cells and tracheæ with bordered pores and simple pits. Crystal fibers containing monoclinic prisms of calcium oxalate frequently adhere to the wood fibers.

## POWDERED DRUG.

Light brown; the characteristic elements being the following: Starch grains which are simple or 2-4-compound (usually 2-3-compound), the individual grains spheroidal, plano-convex, or bi-truncate and up to 15 microns in diameter; numerous calcium oxalate crystals, both as crystal fibers and rhombohedra; numerous fragments of sclerenchyma fibers, the latter often accompanied by crystal fibers containing rhombohedral crystals of calcium oxalate; occasional stone cells with thick, lignified, porous walls; numerous fragments of tracheæ, some of which have bordered pores, others simple pits; resin cells with dense brownish contents.



#### PREPARATIONS.

In addition to the fluidextract, there are two preparations now used mainly by the French. One of these, "Pilula Potentin Composita" contains one grain of extract of muira-puama and one grain of ovolecithin to each pill. It is employed as a nerve stimulant and aphrodisiac in doses of 3 to 6 pills daily before meals.<sup>2</sup> The other preparation "Muiracithin" consists of the residue in vacuo of 100 grams of fluidextract of muira-puama and 5 grams of lecithin with a sufficient quantity of licorice powder added to make 100 pills. The dose given is three to four pills daily; one pill morning and noon and two in the evening.

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## ABSTRACTED AND REPRINTED ARTICLES

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### EMPIRICAL FALLACIES (AND OTHERS).\*

JOHN URI LLOYD, CINCINNATI, O.

Possibly it is proper for one who believes that to empiricism is largely due progress in life's advancement, as both serviceable in the beginning and supplying texts for subsequent research, to call attention to some of the fallacies of misapplied empiricism. A pleasure, is it not, to look back at the errors one held in the passing along of life, and a greater pleasure to utilize such errors for self-reflection and perhaps record them for the benefit of others.

A few years ago this writer, on a special research mission, was traveling through Asiatic Turkey. Observant was he of much that lay outside his direct field of study—many were the pleasurable in-

\*From the *Eclectic Med. Jour.*, July, 1921.

cidents that recollection brings often now to mind, among others the story of "The Blessing of the Fig." With this legend in view, let us consider—

*The Barren Fig Tree.*—The writer observed that early in the springtime certain trees in the fig orchards of Turkey were seemingly far ahead of the great majority of fig trees. Also it was seen that these early fig trees frequented the edges of woodlands and in several instances hedged dividing fence lines as well as thickets along the sides of the road. On these trees the young figs were large before the fruit appeared on the laggards. The writer questioned why this early variety of figs was not more abundantly cultivated. Came the reply that these were barren fig trees and carried no figs to maturity. Came then the story, as follows:

These figs appear early, they grow to a certain size, and open from the rounded apex. From this orifice stream swarms of very small flies, which seek the fruit-bearing fig trees and inoculate them with the spores borne from the fig from out of which they came.

Said my informant: "The fig you have noticed is the wild fig. Its function seems primarily to bear a crop of insects. After these have escaped the fig withers, dies and drops to the ground. The tree bears no fruit; it is barren." In times remote, barren fig trees in an orchard were cut down as cumberers of the ground.

*Mythology of the Barren Fig Tree.*—Continued my informant: "In the early days, the priests, taking advantage of this insect fact not comprehended by the people, appointed each year, as a religious ceremony, a day for blessing the fig trees in the orchards. At that time, as has been stated, the barren fig tree was considered of no value, all being intentionally exterminated from the orchards. A festival day for 'blessing the fig' orchard was appointed for a day when the wild fig was ready to open and liberate the swarm of flies. The priest led the villagers to the wild figs, dressed in holiday attire and bearing branches culled therefrom laden with these figs the procession turned to the fig orchards. As the man of God blessed the fig trees the villagers threshed these trees with the boughs laden with the wild figs. This whipping of the trees of the orchard resulted in the liberation of flies throughout the entire orchard. These flies, seeking the young figs just appearing on the female trees of the orchard, fertilized them with the spores from the wild (barren) fig, and the orchard bore an abundance of figs.

*Empirical Reasoning.*—"What could be more conclusive than that this blessing of the fig orchards by the holy man, and the ceremony performed, resulted in the bountiful fig crop? Self-apparent it was, because fig orchards not thus blessed were comparatively barren.

"We know now," said my informant, "that the wild fig is the male, the fruit-bearing fig being the female, and that the spores that fertilized the fruit were carried from the male to the female fig by the insect that escaped from within the flower of the wild fig. Now, each orchard carries a number of wild fig trees. No longer is the blessing of the priest necessary."

Continued the educated Turk, my companion: "Some years ago came a demand from America for many thousand young Turkish fig trees. These were gathered and forwarded—but," said the Turk, "the Smyrna fig will not be profitably raised until America gets the Turkish insect that, escaping from the young flower of the barren fig tree, accomplishes the fertilization of the fig."

*Apple Trees and Fish.*—When the apple trees bloom in the springtime on the islands of Lake Erie, the bass bite best. The question comes at once to an observing empiricist, "What connection is there between the fish in the water and the flower on the tree?" He might rationally surmise that the influence of the fish makes the tree blossom, or that the blossoms of the tree bring the fish to the shoal. The man of science might perceive that the same warm sunshine that brings blossoms to the tree also entices the fish from the cold depths of the lake, to spawn in the warm water of the shallows.

*Apple Tree and Morel.*—Turn now your attention to the Kentucky apple orchard. Behold, when blooms the apple tree, the morel (an edible fungus) springs in abundance from about the base of the tree. Reasoning empirically, one might say that the bloom of the apple tree awakens the morel from out the earth. Another might perhaps reverse the thought, asserting that the morel's influence makes the apple tree bloom. Simple is this reasoning, but yet the question remains unanswered why the morel rises under the blossoming apple tree and not under the honey-locust but a short distance away.

*Mystery of the Morel.*—Take now this same morel. Go into the deep woodland about the time it appears in the apple orchard.

Search the woodland. No morel is likely to be found until the ash tree is reached, and here it may thickly stud the leaf mould. Within a radius of one hundred feet about an ash tree this writer has gathered a basket of morels, and in the entire woodland, excepting where grew an ash tree, has found no morel. The yellow poplar (*Liriodendron Tulipifera*) also sometimes serves to a lesser degree as a culturing shade host of the morel. Empirical reasoning would say that some influence of the ash tree favors the growth of the morel. Other reasoning might intimate that in times gone by the seed of the ash tree sprouted in a bed of morels, the progeny of which still lingers. The man of science says frankly, "I don't know," but with open mind he perhaps accepts that the root of the ash tree infects the soil with an unknown "something," be it bacteria or secretion, that favors the morel's growth.

*Catalpa and Raspberry.*—When blooms the catalpa tree by the wayside, the black raspberry ripens in the field and thicket. Observing this, the empiricist might say, "The blooming catalpa is the cause of the raspberry's ripening." Another may as rationally differ and argue that ripening raspberries bring the blossom to the catalpa. Judging by facts only, empiricism might thus neglect the heat and light cause that both ripens the raspberry and brings the bloom to the catalpa. The parallel might be extended indefinitely.

*The Black Beech.*—When start the leaves of the "Black Beech," red, even to crimson, dominates. As the season progresses the leaves darken and at last become black. Reasoning from observed facts, the empiricist might argue that a black coloring matter had been deposited in the leaf from which the red had faded. Comes the thoughtful investigation of the man of science. Lo, the black results from a combination of red and green chlorophyll, which in proper proportion makes the black pigment of the matured leaf of the beech. Passes further the scientific investigator, who shows that vegetable green is a mixture of blue and yellow. Did not very primitive people make shades of green by such admixtures? Thus yellow, blue and red makes black to pigment the leaf.

*Clover Fertilizer.*—These many years ago, observing farmers decided that red clover, raised on poor ground, then plowed under, enriched the earth even to fertilization sufficient for a subsequent

crop of wheat. "Imagination," said the chemist, for did not analysis show that clover was insufficient, or even nearly useless, in accepted food content? And yet the farmer was not convinced; he continued to raise clover to enrich his soil. Came then the man with the microscope. Behold, the roots of the clover swarmed with nitrogen-fixing bacteria. To this it might be added that beneath a black locust thicket blue grass luxuriates, and white beans thrive on poor, sandy soil, that mellilotus (sweet clover) asks no fertilizer when it covers Kentucky yellow clay dug from deep in the earth.

*Sun Spots.*—Comes to the sun a mighty "spot" that slowly passes across its face. Simultaneously a display of aurora borealis blankets our heavens. Electrical disturbances pervade the earth, telegraph wires refuse to "message," even lead fuses within brick buildings flash and burn out. What is more natural than to conclude that the earth-phenomenon is caused by the sun spot? But, might not another mind reason that suns and planets are but cells floating in space, and that both sun, earth and heavens respond in unison to an intercellular impulse in the ether that pervades all things?

Remedial agents there are, employed in confidence by observing physicians, though the man of science has not as yet fathomed the secret of their action. Helpless is he to account for phenomena known to his microscope, his biological efforts are fruitless, chemistry fails. The empiricist accepts these facts, he continues to employ the agents discredited by all but those who, by repeated experiences, have learned their uses. With the object of curing his patients, the observing physician walks the forbidden path of an ostracized "irregular."

But enough. None can forever suppress facts with theories, or by means of experiments that do not parallel or cannot fathom Nature's laboratory. The man of science shows why the blessing of the fig trees gave the crop of figs, why the apple blossoms when the bass spawn, why the raspberry fruit ripens when the catalpa blooms; but as yet he closes his eyes in despair and offers no scientific explanation as to why the morel makes its appearance under the apple tree in the orchard and the ash tree in the woodlands, and not in the same rich earth about the base of the beech, the hickory, the elm, the walnut or other trees in the forest shades adjacent to the ash. Such problems as these he will surely work out, and this writer

believes he will yet show how and why a single remedial agent, destitute of toxic qualities and mild to the taste and smell, as is the pith of the sassafras or the fruit of the hawthorn, may stimulate a life process that may change abnormal tissue, excite an exhausted muscle, soothe an inflamed and tender surface, or through some force encourage vitality to restore health.

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IMPROVED DENIGÈS TEST FOR THE DETECTION AND  
DETERMINATION OF METHANOL IN THE PRE-  
SENCE OF ETHYL ALCOHOL.\*<sup>1</sup>, <sup>2</sup>

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The examination of alcoholic products for methanol has been a problem of interest to many chemists. If a certain few published papers are consulted the matter would appear to be rather simple, at least from the qualitative side. But a thorough survey of the voluminous literature, comprising a large number of methods with contradictory comments and conclusions, does not lead one to undertake exacting work along this line with entire confidence.

One of the most recent investigators, Gettler,<sup>3</sup> having reviewed fifty-eight existing tests, recommends subjecting the sample to nine qualitative tests, sequentially applied. In passing it may be noted that his eighth test, a refractometric one, is essentially quantitative in nature, being based upon a numerical difference between physical constants, and is only secondarily of qualitative significance. Also his first seven tests are merely tests for formaldehyde, applied after treating the sample with a single oxidizing agent. If this oxidizing agent is capable of producing formaldehyde from any substance other than methanol, all the seven tests must be subject to a common source of error.

\*From *Jour. of Ind. and Engr. Chem.*, June, 1921.

<sup>1</sup> Received February 16, 1921.

<sup>2</sup> Published by permission of the Secretary of Agriculture.

<sup>3</sup> *J. Biol. Chem.*, 42 (1920), 311.

Purely qualitative findings, however, seldom afford solid ground for action in matters of commercial or legal importance. The question "How much?" is almost certain to arise. It is a pertinent question here, inasmuch as several investigators<sup>4</sup> have stated that methanol is naturally produced in certain fermentations. If methanol, like fusel oil, is a normal constituent of alcoholic products, then the legitimacy of its presence in any case may be satisfactorily settled only by quantitative examination. The analytical chemist needs, first, a simple but dependable qualitative test which shall possess semi-quantitative value in that it is able to serve as a "limit test," and, second, a quantitative method which shall enable him to assert with positiveness very nearly the exact percentage present. The quantitative method must be subjected to intensive study in order:

(1) To develop its highest inherent precision.

(2) To devise methods for the elimination of interfering substances.

(3) In case elimination is impossible, to determine the size of the "blank" involved by the presence of each such substance.

The Denigès<sup>5</sup> test seems most promising for both qualitative and quantitative application. It consists in treating the alcoholic solution with potassium permanganate and acid, whereby methanol is oxidized to formaldehyde. The latter is detected by Schiff's reagent in the presence of sufficient sulfuric acid to prevent development of color from acetaldehyde. There appears no evidence that other proposed oxidizing agents, such as bichromate and acid or persulfates,<sup>6</sup> are inherently superior to permanganate and acid. The latter agent is pre-eminently simple and convenient, requiring no heat for its action and finally affording a colorless solution. No reagent effects a quantitative yield of formaldehyde. All require

<sup>4</sup> von Fellenberg, *Mitt. Lebensm. Hyg.*, 5 (1914), 172; *Biochem. Z.*, 85 (1918), 45; Takahashi, *J. Coll. Agr. Imp. Univ. Tokyo*, 5 (1915), 301; *J. Am. Chem. Soc.*, 39 (1917), 2721.

<sup>5</sup> *Compt. rend.*, 150 (1910), 832.

<sup>6</sup> Preliminary experiments have indicated that persulfates, especially in strongly acid solution, may produce a notable quantity of formaldehyde from pure ethyl alcohol. The possibility of such a reaction has been noted by previous observers in the application of several oxidizing agents. Bichromate and acid, in comparison with permanganate and acid, appears to afford a high yield of acetaldehyde from ethyl alcohol, but a low yield of formaldehyde from methanol.

strict adherence to a standard set of conditions under which it is assumed that a certain concentration of methanol originally present results in a certain concentration of formaldehyde at the end.

Likewise, for the demonstration of formaldehyde there appears to be no reagent any more convenient or reliable than Schiff's reagent, prepared according to the Elvove<sup>7</sup> formula. Its chief comparative disadvantage is the slowness of development of the final color.

#### QUANTITATIVE METHOD.

The Denigès' method has been used with more or less modification by a considerable number of investigators. Since in routine analyses following the procedure of Elvove the observed margin of precision seemed unnecessarily large, the whole process has been subjected to close scrutiny with a view to attaining greater precision. It was decided that 0.04 cc. of total alcohol should be the standard quantity for each test, which, including the necessary acid, should be made to a volume of 5 cc. The nature and proportion of the acid is of very great importance. The highest yield of formaldehyde results from slow action of permanganate in presence of low hydron concentration; but practical considerations prohibit an inordinately long reaction time, while the total acid must be kept up to a safely high figure. The conditions finally chosen were the addition of 0.2 cc. of phosphoric acid (C. P., 85 per cent.), previously diluted to 1 cc. for accuracy in measurement, and an oxidation period of 30 min., instead of the 0.2 cc. of concentrated sulfuric acid and oxidation period of 3 min. employed by Elvove. Next, after deciding that the necessary permanganate should be added in a volume of 2 cc., it remained merely to find a concentration of the permanganate solution such that either more or less than 2 cc. of it would give a lower yield of formaldehyde than exactly 2 cc. The desired strength was found to be 3 per cent. In a similar way the volumes of sulfuric acid and Schiff-Elvove reagent were tested. Directions for the method may be given as follows:

<sup>7</sup> This JOURNAL, 9 (1917), 295. Fuchsin (0.2 g.) is dissolved in 120 cc. hot water. After cooling to room temperature there are added 2 g. of anhydrous sodium sulfite dissolved in 20 cc. water, followed by 2 cc. concentrated hydrochloric acid. The solution is diluted to 200 cc. and is allowed to stand 1 hour before use. If well stoppered in an amber bottle it may remain fit for use for several weeks. The Schiff-Elvove reagent appears decidedly superior to the original Schiff reagent, and should supersede the latter.



Dilute the solution, previously purified as necessary, to 1 per cent. by volume of total alcohol (Sample Solution A). Of this, pipet 10 cc. into a 50-cc. volumetric flask, add 10 cc. of a 4 volume-per cent. solution of pure ethyl alcohol, and make to the mark with water (Sample Solution B). Of the latter, likewise, dilute 10 cc. plus 10 cc. of the 4 per cent. ethyl alcohol to 50 cc. (Sample Solution C). Into 50-cc. tall-form Nessler tubes pipet 4 cc. of the three sample solutions. Prepare standard methanol tubes containing, respectively, 1, 2 and 3 cc. of a 0.04 volume-per cent. aqueous solution of pure methanol plus 1 cc. of 4 per cent. pure ethyl alcohol, plus sufficient water to make 4 cc. After the tubes are properly arranged in a rack the following operations are put through in strict parallelism remembering that each reagent is to be added to all tubes before any are mixed:

1—Add 1 cc. of a 1 in 5 volume solution of phosphoric acid (C. P., 85 per cent.), and mix.

2—Add 2 cc. of 3 per cent. potassium permanganate solution, mix, and let stand 30 min.

3—Add 1 cc. of 10 per cent. oxalic acid solution, mix, and let stand till a clear brown (about 2 min.).

4—Add 1 cc. concentrated  $\text{H}_2\text{SO}_4$  (C. P.), mix, and let stand a few minutes for temperatures to become equal.

5—Add 5 cc. Schiff-Elvove reagent, mix well, and let stand till colors are sufficiently developed (0.5 to 2 hrs.).

Each 1 cc. of the 0.04 per cent. methanol in the standard tubes is equivalent to volume percentages of methanol in total alcohol contained in the sample as follows:

Sample Solution	Per Cent.
A	1
B	5
C	25

For more precise results the determination is repeated on the appropriate sample solution with more closely set standards. The sharpest results are obtained with standard tubes containing not over 1 cc. of standard methanol. To bring the sample into this range it is often best to use only 2 cc. of a sample solution, adding

thereto 0.5 cc. of the 4 per cent. ethyl alcohol and sufficient water to make 4 cc. Approximate readings may be made after 30 minutes, precise ones after 1 hour, but best under 2 hours, for the colors fade later. The limit of detection is 0.2 cc. of the standard 0.04 per cent. methanol.

Tests on four "unknown" mixtures of methanol, ethyl alcohol, and water prepared by an assistant indicated that, including the necessary determination of total alcohol via specific gravity, the results need not be in error by more than 1 part in 20.

#### QUALITATIVE METHOD.

A modification of Denigès' method is official as a qualitative test in the U. S. Pharmacopeia IX. The U. S. P. test has been criticized as unreliable because a false reaction sometimes occurs. Ehman<sup>8</sup> attributes the fault to temperature and overcomes it by running a blank with pure ethyl alcohol, adjusting the temperature until the blank remains colorless. In the judgment of the present writer the difficulty is primarily due to an undesirably high concentration of total alcohol. Since the substitution of phosphoric acid for sulfuric acid considerably more than doubles the yield of formaldehyde from a given amount of methanol, the concentration of the sample in the test here proposed need be only half that employed in the U. S. P. test and still leave the proposed test more delicate than the U. S. P. test at its best. The proposed test has been run at temperatures of 15° and 35° C. without experiencing difficulty with false reactions.<sup>9</sup> It may be conducted as follows:

Dilute the liquid, purified as necessary, to a content of 5 per cent. by volume of total alcohol. To 5 cc. add 0.3 cc. of phosphoric acid (C. P.; 85 per cent.) mix, add 2 cc. of a 3 per cent. solution of potassium permanganate mix and let stand until the permanganate is entirely decomposed (about 10 min.). Add 1 cc. of 10 per cent. oxalic acid mix, and let stand till a clear brown (about 2 min.). Add 1 cc. concentrated sulfuric acid, mix, add 5 cc. Schiff-Elvove reagent, immediately mix well, and observe the color after exactly 10 min. The solution may then possess a pale greenish tint, but should show no distinct blue or violet color against a white background (less than 0.2 per cent. methanol in the total alcohol).

<sup>8</sup> *Am. J. Pharm.*, 91 (1919), 594.

<sup>9</sup> It may be that in the U. S. P. test the presence of sulfuric acid promotes oxidation of ethyl alcohol to formaldehyde at an elevated temperature.

In carrying out the qualitative test it is essential not to be misled by any colors developing in less than 10 min. Concentrated sufluric acid often becomes decidedly weak in the ordinary laboratory reagent bottle, and a transitory color from acetaldehyde may accordingly appear. This is also likely to happen if the Schiff-Elvove reagent is not mixed with the solution immediately after addition. The color arising from acetaldehyde will have disappeared in 10 min. after mixing, but, needless to say, it is a safeguard against error to run a blank along with the test. On longer standing, the test can naturally detect smaller proportions than 0.2 per cent.

#### PURIFICATION OF SAMPLES.

The directions given for both quantitative and qualitative work specify that the original material must be "purified as necessary." In general, the test must never be run directly on any material unless it is positively known to contain only water, alcohol, and other substances known to be innocuous. Alcoholic preparations vary so widely that no entirely general methods of purification may be given. The analyst can generally determine approximately the nature and amount of the non-alcoholic constituents, and must decide whether, in addition to purification, it will be necessary to run a blank on a synthetic mixture.

*Carbohydrates and Glycerol*—These substances, against which Salkowski<sup>10</sup> has given warning, are to be separated by distillation; a step which is also necessary to permit determination of total alcohol via specific gravity.

*Formic and Acetic Acids*—These acids are stated by Rosenthaler<sup>11</sup> to yield color with Schiff's reagent. They can be separated, if necessary, by distillation after neutralization, but the present writer did not find that 10 per cent. by volume of either acid added to pure ethyl alcohol produced any color by the qualitative test.

*Formaldehyde, Terpenes, Etc.*—These impurities are removed by von Fellenberg<sup>12</sup> by treatment with sodium hydroxide and silver nitrate, followed by distillation.

<sup>10</sup> *Z. Nahr.-Genussm.*, 28 (1914), 225.

<sup>11</sup> "Der Nachweis organischer Verbindungen," 1914.

<sup>12</sup> *Biochem. Z.*, 85 (1918), 45.

*Phenol*—As noted by Scudder,<sup>13</sup> phenol interferes with the test to a degree dependent on its concentration. It may probably be adequately separated by distillation after addition of a liberal excess of caustic alkali.

*Fusel Oil*—This has been stated<sup>14</sup> to afford a slight false reaction after oxidation. The present writer obtained one sample of "fusel oil," and two of C. P. amyl alcohol (rectified fusel oil), one of the latter being an "analyzed reagent," all from different manufacturers. Each sample was made into a 10 volume-per cent. solution in pure ethyl alcohol, and the qualitative test was applied. The heaviest color was given by the presumably purest sample, namely, the "analyzed reagent." Upon making the qualitative test quantitative by running it in comparison with known mixtures of methanol and ethyl alcohol and letting stand an hour or more, the color produced was found markedly fainter than the color produced from ethyl alcohol containing 0.08 per cent. methanol. By the regular quantitative test the color was indistinguishable, being clearly less than the equivalent of 0.1 per cent. methanol. Hence the present writer has been unable to demonstrate interference by fusel oil, provided that it be not attempted to strain the test beyond the limit recommended, namely, 0.2 per cent.

*Acetone*—This ingredient, constituting up to 10 per cent. of the "total alcohol," does not appear to affect significantly qualitative or quantitative results.

#### SUMMARY.

The Denigès test has been modified to increase sensitiveness and precision, and is recommended for practical work in the detection of, and especially in the quantitative determination of, methanol in the presence of ethyl alcohol, inasmuch as the possible normal presence of methanol in alcoholic products renders purely qualitative tests unsatisfactory. Though capable of greater refinement, the tests are adjusted to a minimum limit of 0.2 per cent. methanol in total alcohol. Procedures for the removal of certain interfering substances are outlined.

<sup>13</sup> *J. Am. Chem. Soc.*, 27 (1905), 842.

<sup>14</sup> von Fellenberg, *Biochem. Z.*, 85 (1918), 45; Salkowski, *Z. Nahr.-Genussm.*, 36 (1918), 262.

## A HALF CENTURY OF AMERICAN PHARMACY.\*

(Address of Prof. H. V. Arny, Columbia University, at the Jubilee Celebration of the Ontario College of Pharmacy.)

It is a great honor and privilege to bring to the Ontario College of Pharmacy upon this memorable occasion the greetings of the pharmacists on the other side of the Great Lakes. The name "Canadian" has taken on new meaning to us living under the Stars and Stripes since your brave sons fought on Vimy Ridge and reddened even the poppies on Flanders fields. With naught but the St. Lawrence, the Lakes and a few thousand miles of imaginary line separating us, our countries, peaceful neighbors for over a century, became comrades in arms for eighteen of the War's fifty-one tragically glorious months; so soon, alas! forgotten in certain quarters.

To refer to the occasion we celebrate, it is a great thing for an organization to have weathered the changes and chances of half a century. It is a matter worthy of the most cordial congratulations that this organization has attained the vigorous fifties with so fine a record of achievement. May the coming fifty years of the Ontario College of Pharmacy be of even greater success than the half century just drawing to a close.

We pharmacists in "The States" have been celebrating to quite an extent during the past year. Just one year ago the oldest State Pharmaceutical Association, that of New Jersey, celebrated its semi-centennial, while this very week, the oldest College of Pharmacy in America, that in Philadelphia, is holding its one hundredth graduating exercises.

Since 1920-21 has been a year of celebrations, it is well to pause a few moments to look back over fifty years with the hope of gaining from the past lessons for the future. Pharmacy has been far from quiet during this half century. Let us see whether its activities have been for good or evil.

Let us imagine ourselves back in 1871 when the Ontario College of Pharmacy was organized. My childhood memories of the seventies hover around a fine old town at the other end of the country from whence I come, New Orleans; washed by the Father of

\*From *Canadian Pharmaceutical Jour.*, July, 1921.

Waters, and fanned by the breezes from the Gulf of Mexico. Far away though it is, I doubt whether the drug business down there was much different from that plied up here. I recall a fine old druggist named Pope, with a choice store in a select neighborhood. An attractive store it was, with white wall fixtures upon the shelves of which were rows of bottles with gold labels bearing mystic names; with narrow white counters surmounted by small show cases made of panes of ordinary glass, fastened together by wooden frames; with the dispensing counter and the soda counter possessing the "novelty" of marble slabs; with a soda fountain made of marble, shaped like a cottage, or a barn. In the rear there was a room from whence mysterious noises and still more mysterious odors proceeded; the noise of the clanging pestle against the iron mortar, a symphony I was destined to produce many times a decade or so later; the odor of wild cherry, of aloes, of turpentine and of valerian. There was another drug store, that of Dr. Hastings, that enthralled me still more, for from it proceeded an odor that blended all of the mystery of centuries of incantation and drug magic. The memory of that odor clung to me until my student days; when delving in the stinks of chemistry, I recognize my old friend of the Hastings pharmacy in *Mercaptane*. Here is a clue for the pharmaceutical historian. Did Dr. Hastings anticipate sulphonal and its congeners? Before the historian goes too far in this quest, I might add that I understand that Dr. Hastings had installed upon his premises an apparatus for making his own illuminating gas.

Then there was in New Orleans in the seventies the drug store of Thomas Finlay, a well-trained pharmacist, the great prescriptionist of the English-speaking medical men; a store from whence sprang his nephew, Alexander K. Finlay, thirty-ninth president of the American Pharmaceutical Association. Across Canal Street, the mystic line separating the New Orleans from the old; in the old French quarter famed in song and story, there were *pharmaciens* of ability and of worth; there were drug stores that rarely came before the eyes of the American boy now telling you the story. There were Laplace, Cusach and Robin, leaders among their pharmaceutical *confreres*.

And now to jump from the Gulf to the Lakes, from the land of the palmetto to the land of the maple, I leave to you, who know better than I, the picturing of those goodly men of the Province of

Ontario who founded your college; blood brothers of the Popes, the Hastings and the Finlays of far-off New Orleans. Of these worthies the one whom we of the United States hold in grateful remembrance was your William Saunders who, in 1871, was active in manufacturing pharmacy; a constant exemplar of the fact that a pharmacist is an educated man. Twenty-fifth president of the American Pharmaceutical Association, Dr. Saunders has always seemed to us of the United States, the personification of Canadian Pharmacy. Others there are, to be sure, to whom we turn with like esteem, but since some of them are present tonight, I will spare their feelings by permitting the name of Dr. Saunders to stand alone.

From the apothecaries of 1871 let us turn to the pharmacy of the same period. In these days the art of dispensing meant more than it does in the drug store of 1921. The spreading of plasters was an every-day occurrence, and apothecaries took pride in showing their skill in preparing those of unusual shape. Machine-spread porous plasters brought out in 1847 by one patent medicine manufacturer, were still novelties from the dispensing standpoint in 1871. Pills were made by hand by the druggists in quantity lots. Even thirty-seven years ago, when I began my pharmaceutical apprenticeship, we made all of the pills (such as compound cathartic and quinine) that were sold over the counter; the only coated pills we dispensed being proprietaries or special lines prescribed by physicians because of the advertising activity of their manufacturers. Compressed tablets, introduced into American Pharmacy by Jacob Dunton, of Philadelphia, during the late sixties, were being pushed by a few manufacturers but were dispensed by apothecaries only upon the prescription of the physician who specified them. Tinctures were the staple form of drug medication; fluid extracts being then new and of lesser importance. Mixtures were prescribed largely and were freshly prepared by the apothecary. Malodorous milk of asafœtida and its sinister sister, Dewee's Carminative, were in great demand, and a fine job it was to make the former when one, all dressed up, on one's Sunday off, came back to relieve the employer or the brother clerk over the dinner hour. Emulsions of fixed oil were in their infancy a few stray recipes for cod-liver-oil cream being found in the literature of 1870-71. Elixirs were then in their first flush of popularity, with those dispensing them little

dreaming that within a half century they would command the attention of Prohibition officials. Hypodermic medication was an entire novelty that was much discussed in the journals of half a century ago, and it is obvious that serum medication was unknown; in fact the word "antiseptic" was used but seldom and "the new germ theory of disease" was the subject of an address before the British Association in 1870.

As to drugs, eucalyptus was a novelty; while cascara-sagrada was unknown; strophanthus was of interest only as an African arrow poison. In the chemical field, among the "new medicines" we find chloral, phenolsulphates and potassium permanganate. The German tar barrel had not yet started to turn out antipyretics and hypnotics and antiseptics for the healing of nations and for the filling of German purses. Phenol, of course, was used, the famous brand of that time being that of the English house of Calvert, who brought forth their first pure product in 1863.

Medical thought of half a century since was immensely different from that of today. With the germ theory in its infancy, with antiseptics merely a matter of chance, with toxins and antitoxins unknown, the physician had to depend upon drugs and chemicals and that, it must be admitted, in a rather hit or miss fashion. Homœopathy was under serious discussion, both in the English and American pharmaceutical press; since it was viewed both by the regular physician and by the apothecary with a feeling akin to alarm. The Hahnemannian school has exerted considerable influence, although not in the way that was anticipated in 1871. It had its part in turning physicians of the regular school from the nauseatingly bitter mixtures of those days to more palatable preparations; it had its effect in persuading the old line medical men that reasonably small doses frequently repeated are often of more service than the occasional administration of heroic doses; it may have inspired the therapeutic nihilism of the ultra-modern teachers of medicine; a philosophy the logical sequences of which are the healing cults such as Eddyism.

Whatever its influence upon the regular practice of medicine, homœopathy has had a decided effect upon the practice of pharmacy. Practitioners of the regular school, feeling the competition of the homœopathic physician with his satchel of sugar pills, began dispensing instead of writing prescriptions. The tablet industry, in



its infancy in 1871, has, during the half century since that time, assumed enormous proportion in supplying the needs of the average dispensing physician and tablets have now become as staple as ground flaxseed. If the tablet vogue continues there may be some day an automat, doctors and druggists rolled into one, in the form of a nickel-in-the-slot machine, dealing out tablets for all sorts of ailments. Already around New York tin boxes containing a well-known brand of acetylsalicylic acid tablets are being sold at news-stands. With the lessening of the prescription business the pharmacist has had to turn to other means of paying his constantly increasing rent and as a result, in the cities at least, the old-fashioned drug store has given place to a handsome emporium in which the dispensing of medicine seems the least part of the business. And then, forsooth! the physician, intentionally overlooking the causes of the commercialization of pharmacy, throws up his hands in holy horror over the modern drug store and thus justifies his neglect of the art of prescription writing.

This is the situation, but that it is not so gloomy as the pessimist may think, the presence of you prosperous gentlemen at the semi-centennial of your organization seems to attest. Nor do I believe that your prosperity has been due solely to the sale of apples, of cameras and of sandwiches. The remarkable growth of schools of pharmacy, including your own fine institution, shows that there still remains an art of pharmacy, a science of pharmacy, and a profession of pharmacy. Did I not think so I would consider that I was obtaining money under false pretenses in accepting my salary as teacher, and I would turn to the business of pharmacy rather than remain in the ranks of the teachers.

We have considered the past and the present of pharmacy. How about the future of Pharmacy? I am an optimist and can say with Rabbi Ben Ezra:

"Grow old with me  
 The best is yet to be,"

and so I have no fear that the future will see relegation of pharmacy to the things of the past along with astrology, alchemy and necromancy.

That a man of indifferent education and mediocre ideals will be naught but a tradesman in pharmacy, even as an indifferent

farmer will be naught but a hewer of wood, a drawer of water and a digger of ditches, goes without saying. But if a pharmacist has the vision, not necessarily of "The Glean" that Tennyson writes about, but a view of the broad expanses of opportunity before him, that man will not only be an exponent of real pharmacy, but will also be a successful pharmacist.

Let me give a few illustrations of what I mean. Here is one pharmacist I know who is famed in the city where he lives as having the one apothecary shop where all sorts of finely garbled herbs are available; not the compressed packaged herbs that are seen in most stores, but carefully dried herbs almost as handsome as herbarium specimens.

Here is another retail pharmacist, a Bell scholar, by the way, who is gaining reputation throughout the United States for the digitalis preparations standardized by the Hatcher method.

Here is a Southern druggist who, having a bent toward chemistry, specialized in making unlisted chemicals for those physicians desiring them, thereby adding to his daily receipts and to his reputation among the medical fraternity.

Here is a New York pharmacist who dared to specialize as a prescriptionist, who prepared himself to dispense sterile medications in ampule form, and who now has people coming to his store from all over the big city, asking for special prescription work of highly technical character; ready to pay the adequately high price that such service means.

Here is an apothecary in a city on the Great Lakes, who, despite the enormous number of thyroid preparations on the market, has built up quite a business in dispensing, in capsules, dessicated thyroids sent to him in fresh condition from the slaughter house. It is needless to say that this man has the finest prescription business in his city.

Here is the pharmacist (now numbered by scores) who, starting in by performing in a satisfactory manner urinary work for the medical profession, has developed that side-line into a busy laboratory where the chemical and bacteriological side of clinical diagnosis is performed at fees commensurate with the service.

And lastly, let me cite by name one pharmacist, who showed us of the United States, the possibilities of professional pharmacy, that great pharmacist, Henry P. Hynson, of Baltimore, whose de-

mise on the 19th of last April brought sorrow to all of his co-workers in the American Pharmaceutical Association. No higher tribute can be paid Dr. Hynson than the following paragraph taken from an editorial published in a recent number of the *Journal of the American Medical Association*:

"As already suggested, his constant effort was to emphasize as of primary importance the service which the educated scientific pharmacist was in a position to render to the public, and to decry the commercial ideas which seemed to be strangling the professional instincts of the pharmacists. He opposed commercial drug store exploitation of the public with 'patent medicines' and making pharmacy a mere adjunct to the sale of soda water, light lunches and novelties. Hynson was one of the few prominent pharmacists who were willing to forego financial gain in order to raise the ethical standards of a profession which he honored. He took an earnest interest in all the live pharmaceutical questions of the day, and pure pharmacy sustained a great loss in his death."

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## THE RELATIVE VALUE OF THE PROTEINS IN NUTRITION.\*

By R. H. A. PLIMMER.

Complete hydrolysis of the protein to its constituent 18 or 20 amino-acids occurs during digestion in animals; the amino-acids circulate in the blood and reach the various organs, which build up new tissue from the units. Animals have been maintained on a diet containing as its protein content a mixture of pure amino-acids in suitable proportions. Biologically, the proteins must therefore be regarded as mixtures of the various amino-acids, digestion and absorption as a re-shuffling of the units. The amino-acids are not convertible into one another, nor capable of being synthesised by the animal organism, with the exception of glycine, which, under certain conditions, can be formed in the body. The different proteins have different compositions, thus, for example, casein contains 16 per cent. of glutamic acid and gliadin 40 per cent. Some proteins are complete, *i. e.*, contain all the amino-acids, others are incomplete and lack certain units. It can thus hardly be expected that proteins should have the same value in nutrition. Some of the

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amino-acids may be indispensable, others not so essential. There are two main problems to study in nutrition: the formation of new tissue, as in the growth of young animals, and the maintenance of tissue, which undergoes so-called wear and tear, in adult animals. The problem is ultimately to find out the function of each amino-acid in growth and maintenance.

#### THE EFFECT OF THE ABSENCE OF CERTAIN AMINO-ACIDS.

The most certain way of studying the problem is to feed animals upon known mixtures of amino-acids, but the practical difficulties are far too great. The amino-acids are not easily prepared, and it is almost impossible to obtain sufficient of each of them to feed an animal, even a mouse, for any length of time. Two other ways are possible:—(a) To feed incomplete proteins and add the missing unit or units; (b) to feed completely hydrolysed proteins, *i. e.*, a mixture of amino-acids from which one or more units have been removed by chemical means.

The first experiment of this kind was made by Willcock and Hopkins in 1906. Zein was chosen as incomplete protein and fed to mice: in one set alone, in another set with the addition of 2 per cent. of its amount of tryptophan. Failure occurred in both sets of animals, but not so rapidly in those on zein and tryptophan. Young mice with zein alone died generally in 16 days; with zein and tryptophan in 30 days. Adult mice without tryptophan lived 27 days, with tryptophan 49 days. The survival period was thus appreciably lengthened by the presence of tryptophan. The failure to live was most probably due to the absence of other units from the zein. Ackroyd and Hopkins repeated the experiment in 1916 by the second method of experimenting which offers better conditions. The animals were fed upon a mixture of the amino-acids from casein. This mixture does not contain tryptophan, since it is destroyed by acid hydrolysis. In the first period tryptophan was added; on the twelfth day it was omitted and introduced once more on the thirty-fifth day. The animals continued their growth during the first period, declined in weight during the second period, and grew again in the third period when the tryptophan was present.

Osborne and Mendel in America have made numerous experiments with various pure isolated proteins of known amino-acid composition. Their most important results in this connection were

with wheat gliadin; this is a complete protein, but has very little lysine. Adult rats were maintained for long periods on this protein—as long as 500 days—but young rats, though they lived for long periods, failed to grow. The authors therefore regarded lysine as essential for growth. Later, they showed that if they added lysine at definite intervals to the food containing gliadin as sole protein, growth took place with the lysine, but not without it. The minimum amount of lysine necessary to produce normal growth was found to be between 2 and 3 per cent. of the amount of protein in the diet.

The value of lysine for growth was shown in a more practical way by Buckner, Nollau and Kastle. They fed chickens on a poultry farm on diets of high and low lysine content. Their figures and photographs definitely showed more rapid growth on the mixture of high lysine content.

The two other hexone bases—arginine and histidine—are essential units of proteins. As shown by Ackroyd and Hopkins, their removal from the hydrolysed casein mixture leads to loss of weight of the animals; if only one is absent from the food the rate of growth is lessened, so that it appears as if these two units were inter-related. The structural formulæ of these compounds suggest a possibility of the conversion of the one into the other by the wonderful mechanisms of the animal body. These two units were found to give an increase of allantoin in the urine of the animals; thus we know that the purine ring can be synthesised from them. This synthesis by animals has long been suspected, as young birds and animals produce purines on a diet with an almost complete absence of purine compounds.

It is more difficult to arrive at the function of the amino-acids containing aromatic nuclei. Some proteins lack tyrosine, but all contain phenylalanine, which is very difficult to remove from a mixture. Phenylalanine and tyrosine both give rise to homogentisic acid in cases of *alkaptonuria*; phenylalanine may therefore be oxidisable to tyrosine in the body. The almost complete removal of tyrosine from the mixture from casein made no difference to the growth of rats, as shown by Totani. The amount of phenylalanine in the mixture was thus probably sufficient to supply the need for aromatic nuclei. According to Abderhalden, tyrosine cannot be dispensed with.

Cystine is the only unit which contains the element sulphur, though another sulphur-containing compound may be present in proteins. The amount of cystine is not known except in a few cases, but it is estimated from the sulphur content. The need of cystine in the food has been shown most conclusively by experiments with phaseolin, the protein of the navy bean. Slow growth resulted on a diet with the protein alone, but normal growth followed the addition of 2 per cent. of its amount of cystine. Very little sulphur is present in casein. Osborne and Mendel found that less casein was required in a diet if it were augmented with cystine: 15 per cent. casein alone gave normal growth, but 9 per cent. if cystine were added.

It is not possible to test a protein without proline, but arachin with only 1.4 per cent. was tried by Sure. This protein failed to give normal growth even after the addition of extra proline, so that its deficiency must be caused by another missing substance. It is possible that proline and glutamic acid are related units in the molecules of the proteins.

An experiment has also been made to see if the animal organism can introduce an amino group into the molecule of nor-leucine and convert it into lysine. Animals fed upon gliadin and nor-leucine did not grow just as on gliadin alone. The synthesis is thus not possible.

The whole group of simple mono-amino-acids has yet to be tested. They may not all be necessary. In cases of diabetes several can give rise to glucose; their function may be to supply energy through their conversion into sugar. Isoleucine is absent from gelatin, as recently shown by Dakin; this may be another reason for the failure of gelatin in nutrition, which is usually attributed to the absence of tyrosine, cystine and tryptophan.

#### COMPARATIVE NUTRITIVE VALUE OF PROTEINS.

Few proteins show such marked deficiencies as gelatin, gliadin and zein. The different amounts of the units in complete proteins make little difference to growth if the diet contain *abundance* of protein. Growth is observed on the most varied proteins of animal and plant origin; but if any *restriction* in the amount of protein in the food be made, then the growth is lessened or inhibited. Each complete protein will thus have a definite minimum for growth.

Two per cent. lactalbumin gave maintenance, 4.5 per cent. growth; 2 per cent. edestin scarcely gave maintenance, 4.5 per cent. slight growth; with other proteins 2 per cent. led to loss of weight. With a protein content of 4.5 per cent. the best growth was with lactalbumin, followed by edestin; there was no growth with casein unless supplemented with cystine, or with glycinin or squash-seed globulin. An experiment showed that a food with 9 per cent. of lactalbumin was equal to one with 12 per cent. of casein or with 15 per cent. of edestin.

#### THE NUTRITIVE VALUE OF THE PROTEINS OF LEGUMES, NUTS, ETC.

The legumes contain large amounts of protein, and the chemical analysis of the proteins shows no abnormality. The proteins of the pea have been found inadequate by McCollum; it is probably due to lack of cystine, for, as stated above, phaseolin is supplemented by cystine.

The soya-bean protein is of good quality for normal growth, so also are the proteins of the peanut. The latter are peculiar in their high lysine content. The proteins of these foods require cooking so as to make them capable of being digested and assimilated.

The edestin of hemp-seed and cotton-seed is not a perfect protein with its high arginine and glutamic-acid content, but the food-stuff is largely used in America as cattle food. Its poisonous constituent can be removed by steaming or by the hot method of oil extraction.

Nut proteins have a high value on account of the high proportion of hexone bases which they contain. Normal growth has been observed on coconut press-cake, walnut, filbert, pine nut, and other nuts. Experimental work has thus confirmed the assertion of fruitarians of the high value of nuts in nutrition.

#### THE NUTRITIVE VALUE OF THE MIXTURE OF PROTEINS IN CEREALS.

Though the gliadin group of proteins of cereals is not adequate as source of protein in the food, it does not follow that the mixture of proteins in the grain is likewise insufficient. Wheat and maize glutenins as sole protein have been found satisfactory for growth, and may compensate for the inefficiency of the gliadins. The whole grain contains also small quantities of an albumin, globulins, and proteose. Particular attention has been paid to the nutritive value of cereals. The results are not altogether consistent; the

discrepancies seem to be due to the different basal diets used by the various investigators. The results of McCollum and associates are very contradictory; they believe the inadequacy depends on improper mineral supply. Insufficiency of vitamin supply is a contributory cause. Osborne and Mendel tried not only the whole grain, but also different commercial articles produced by milling, such as wheat flour, bran, embryo. Normal growth followed the use of whole grain, and very little difference was noticed among the various grains.

In all cases animals kept for long periods produced small or no litters of young; their health had thus been impaired. This loss of reproductive power has been observed by all workers if cereals supply the sole protein.

Wheat embryo contains the albumin, and is fully adequate; bran proteins are even of superior value. Wheat flour, pearl barley, and maize meal are not adequate.

The milling process thus removes "good" protein. Wheat flour, etc., does not contain enough total protein, but in the experiments the total was made up by adding gluten. The endosperm of the grain will only furnish protein for maintenance.

#### SUPPLEMENTS TO THE PROTEINS OF CEREALS.

Neither men nor animals consume the whole cereal, and as the endosperm does not supply enough protein in quantity or quality, it must be supplemented. The protein ratio of 1:10 needs to be increased up to 1:5. Animal proteins form the best supplements. Lactalbumin was shown by Osborne and Mendel to be the best supplement, but for some peculiar and unaccountable reason other workers do not find this protein so good. Meat, milk, eggs are almost equally efficient, but casein is of less value. In the case of maize meal and milk at least an equal part of skim milk is needed; this gives 30 per cent. of the mixture of proteins as derived from milk. Yeast protein and peanut flour are good supplements. Cottonseed and pea are inferior, whilst products like distillers' grain or vegetable albumin, which is derived from grain, are of little value. The best supplementing proteins are thus those containing the hexone bases, tryptophan, etc. which are low in amount in the cereals.

To produce normal or rapid growth it is possible that it may be more economical to use "good" proteins, which are more expensive than "bad" proteins.



#### QUALITY OF PROTEIN IN MILK PRODUCTION.

Diet plays a large part in milk production. Quantity and quality of protein are the chief factors. Since neither the animal body nor the mammary gland can synthesize amino-acids, the food must contain sufficient for the manufacture of casein and lactalbumin. Hart and Humphrey have paid some attention to this question. A high milk yield of 27 lb. requires a protein ration 1:4.5; 1:6.7 is necessary for 11 lb.; 1:8.5 is not economical. If the animal is not furnished with sufficient protein it produces milk from its own tissues. Skim milk has an efficiency of 65, against 25 of a mixture of maize and alfalfa. Gluten feed (maize embryo) has 45, flax seed 61, casein 59, milk powder 60. A comparison of clover and alfalfa on the same basal diet showed a superiority of alfalfa for high milk production for 16 weeks. With another basal diet the reverse may be the case. The value will depend on the proportions of the amino-acids in the food and their correspondence to the proportions in the milk proteins. No guide is at present available from the side of chemical analysis. Little is known of the proteins of grasses and green foods. The nearest approach to the proteins of cow's milk are the proteins contained in the milk of other animals. If the milk proteins of all animals are the same in composition, the milk of one animal will be as good as that of another animal, but if not, as is most likely, the best source is the animal's own milk. Cannibalism has been proved to be the best method of feeding dogs. We approach cannibalism in the nursing of the young on mother's milk. Milk contains ultimately the proteins of the mammary gland.

#### PROTEINS AND PELLAGRA.

The primary cause of the disease pellagra appears to be quality of protein, but at the same time insufficiency of protein together with improper salt supply may play a part.

Pellagra was not recorded in Europe before the introduction of maize into Spain by Columbus. The disease spread to France, Lombardy and eastwards, wherever maize was extensively used for food. Roussel (1866) cured it by good food, and advanced cases have been successfully treated by a generous diet (Lorentz, 1914; Willets, 1915). Goldberger cured and prevented the seasonal appearance of pellagra in lunatic asylums by increasing the meat and milk in the diet, which had previously been very deficient in this

respect. Goldberger produced the disease experimentally in a squad of volunteers by a diet consisting of vegetable protein, mainly wheat, maize and rice. On a vegetable diet principally of maize, Click and Hume produced symptoms in monkeys very like the symptoms of pellagra in man, and a cure was effected in one case by a diet containing better proteins.

Wilson, of Cairo, who investigated the outbreaks of pellagra in Armenian refugee camps at Port Said, found the diet was inadequate in energy supply and protein supply (vegetable). Thomas (1909) tested the comparative values of proteins for man, and found that meat was three times as good as maize. Wilson, calculating from Thomas' figures, determined that the refugees had a casein equivalent of 22 gm. per day. On improving to a casein equivalent of 41 gm. per day no more cases of pellagra occurred. Shortage of protein and quality of protein are thus at the root of the trouble.

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## AN IMPROVED METHOD OF PRESERVING SPECIMENS FOR A HERBARIUM.\*

By E. A. PRICE AND NOEL L. ALLPORT.

The procedure generally adopted for the preservation of botanical specimens leaves much to be desired. The flowers are simply introduced between sheets of absorbent material, such as blotting-paper, and subjected to pressure, either in books or the botanical press. The process is long and tedious, requiring not less than three weeks to complete; it necessitates repeated changing of the absorbent sheets, and since the tissues become flimsy the risk of distortion is very great; in wet weather the plants must be first freed from external moisture; finally there is the liability to infection by mould. Even when these difficulties are overcome the resulting specimens lack permanence, both of shape and color. Particularly is this the case with members of the *Orchidaceæ*, which become wrinkled and assume a dirty brown tint; again, aquatic plants, such as *Hottonia palustris*, cannot be induced to retain the delicate coloring of the leaves and flowers.

\*From *Pharm. Jour. and Pharm.*, July 2, 1921.

#### THE IMPROVED METHOD.

The improved method about to be described, while being exceedingly simple and calling for no elaborate apparatus, is free from almost all the disadvantages cited above. About one and a half hours will usually suffice to complete the whole operation; the characters of the flowers, including the delicate gradations of color, are permanently preserved; the actual manipulation of the process is much easier than is that of the old method; and after a little practice the procedure can be relied upon to work on all occasions. It may be particularly noted here that the different shades of green in the leaves, which are so rarely maintained in their true contrasts, are satisfactorily preserved in collections treated in this way.

The plant is first placed between about twelve sheets of white blotting-paper, so that there are six sheets above and below. It is then gently pressed with a moderately warm domestic flat-iron of about two pounds weight. The iron should be kept constantly moving. The temperature of the iron is, of course, an important consideration. The best gauge is experience. If the metal is too hot the coloring matters of the plant, particularly the chlorophyll, will be decomposed, and the specimens thus rendered useless. On the other hand, if the temperature is inadequate the permanency is impaired and the plant becomes brown; this is possibly due to the fact that the contained enzymes have not been inactivated. As a rule the growth of enzymes is rapidly inhibited by exposure to a temperature of 70° C. The heat applied should be sufficient to cause water vapor to rise through the blotting-paper as the moisture of the plant is dried out. We suggest that 110° C. would not be very far wrong. Floral collections thus treated are no longer flimsy, but dry and rigid, yet otherwise retaining their natural appearance. The liability of the blotting-paper containing chemical impurities with disturbing influences is not great, but it should, nevertheless, be recognized as a possibility. All paper is bleached with calcium hypochlorite, and if any traces should remain in the material used for pressing plants the colors of the tissues may be altered. If any trouble is met with in this direction another brand of paper should be tried.

Immediately after preservation in this manner the specimens should be painted over with a dilute solution of mercuric chloride in absolute alcohol, a suitable strength being about 0.5 per cent. This

will render them impervious to attack by parasitic insects and moulds. It will not be appropriate to offer a few observations on the mounting of the plants. The most satisfactory support is Whatman's thick, white cartridge paper, such as is used by artists for sketching. The ordinary gum of commerce frequently contains sulphurous acid added as a preservative, and should therefore not be employed as an adhesive, since it is liable to bleach the plant colors. The best mountant is a mucilage of the pure gum acacia of the B. P. to which has been added a few grains of Beta-naphthol to prevent its decomposition. This preparation has the advantage of being free from chemical impurities, is firmly adhesive, and is invisible. It will be shown later that it is sometimes advisable to divide a plant into its component parts before preserving, and where this has been done the general rule for mounting is to fix the main axis and foliage leaves to the paper support first, then the inflorescences can be easily fitted in their correct positions. The tissues being strong and inflexible after the preservation treatment, there is no difficulty in reassembling the parts. Dissections illustrating the constructional characteristics may be mounted beside the complete plant. The liability of these component parts to fade and crinkle is avoided by the new method, thus overcoming a time-honored difficulty. Thus, excellent illustrations of the primrose can be made exhibiting the pin-eyed and thrum-eyed varieties and their adaptability to cross-fertilization. It was noticed that when this ironing process is employed the liability of the dissections going green is obviated. With large flowers and leaves the adhesive may be applied to the back of the plant itself, while for small examples it should be spread on the paper only. When the paste has been applied and the specimen fixed in position it should be firmly pressed with a soft cloth to ensure the removal of air bubbles which tend to form under the leaves, and if ignored at this stage will give the plant a wrinkled appearance when it is dry. We possess a collection preserved and mounted as detailed above that has retained the color of both flower and foliage during a period of eight years.

Certain orders of plants demand special treatment to which our process is readily applicable. A few examples will be mentioned and will serve to demonstrate the practical possibilities of the method.

COMPOSITÆ.

It is necessary with flowers of this order to gently flatten the disc florets to the same level as the ray florets by applying the apex of the flat-iron to the former before giving the general pressure to the whole specimen; otherwise, of course, the ray florets will be shrivelled.

ORCHIDACEÆ.

As is well known, these flowers consist of massive tissue, and it is often advisable to remove the perianths and press them separately. They can all be detached first by cutting across the ovary and then mounted on to the remainder of the plant afterwards. With the exercise of a little care it is impossible to detect that any separation has been made. Such specimens as *Ophrys apifera*, *Ophrys muscifera*, *Cypripedium calceolus* and *Listera cordata* can thus be preserved with every detail of their natural color permanently retained, which is extremely difficult, if not impossible, by the old method. It may be noted generally that in all big flowers the preservation of the smooth texture and natural color of the corolla, or perianth, is greatly facilitated by dividing from the main axis, then preserving and mounting separately.

SPECIAL FLOWERS.

Such special flowers as *Drosera rotundifolia* and *Pinguicula vulgaris* respond admirably to the ironing process. It is possible to preserve them with the insects caught by the plants, *in situ*. If the leaves of the former are treated separately, specimens can be prepared demonstrating the glands bent over towards the insect situated on the leaf surface; at the same time the delicate shades of red and green are retained. In preserving a plant such as the *Paris quadrifolia*, the advantages of the new process are very manifest. By the original methods the contrasting greens become a dull monochrome, whereas it is possible by the procedure described to permanently preserve the delicate greens of the perianth, the yellow anthers, and the shades of purple in the ovary and stigmas.

VIOLACEÆ AND IRIDACEÆ.

Some plants, such as most members of the *Violaceæ* and *Iridaceæ* will probably lose their color quite irrespective of the method employed. The plants, after this new treatment, are, however, so hard and firm that a way of overcoming the difficulty was found.

After preserving and mounting as described, the coloring matter from several flowers of the same species was extracted with absolute alcohol, and the liquid thus obtained was used to paint the specimen intended for the herbarium. In this manner an example of *Iris pseudacorus* has the appearance of having actually retained its yellow color.

In conclusion, we would commend this new method to those who have suffered many disappointments in endeavoring to make a satisfactory herbarium by the old system of continued pressing. The process here explained has been tried and proved, and we are able to claim for it that it not only gives more gratifying results, but that it is also easier to manipulate.

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## THE TITRATION OF CERTAIN ALKALOIDS.\*

By NORMAN EVERS, B. Sc., F. I. C.

In examining the literature of analytical chemistry in the light of modern development of the theory of titrations one is struck by the haphazard way in which indicators are recommended for titrations. Most frequently indicators appear to have been chosen on account of the sharpness of the end-point rather than on account of suitability on theoretical grounds for the titration in question. Further, the indicators used are chiefly confined to methyl orange, phenolphthalein, litmus, and cochineal no one of which, with the exception of phenolphthalein, can be regarded as a good indicator when compared with the new and brilliant indicators which are now available. Probably the chief reason why these new indicators are not in more common use is the absence of any data as to the titrations to which they are applicable.

### THEORETICAL CONSIDERATIONS.

In a theoretically perfect titration of a weak base, such as morphine, we should run in standard hydrochloric acid until we had in our solution nothing but pure morphine hydrochloride. The means by which we determine when the morphine is in the state of hydrochloride is by adding an indicator. Now all indicators change,

\*From *Pharm. Jour. and Pharm.*, June 18, 1921.

in color over a definite range of hydrogen ion concentration—that is to say, the change of color of an indicator is brought about by hydrogen ions, and what we are actually doing when we bring a solution to the neutral point of methyl orange, say, is to bring it to a definite hydrogen ion concentration. Therefore, if we add methyl orange to our morphine titration and bring the solution to the neutral point we are bringing the solution to a hydrogen ion concentration of about  $^1P_H = 4$ , or, if we use cochineal, to about  $P_H = 6$ . Now if the hydrogen ion concentration of a solution of morphine hydrochloride of the strength used in the titration is  $P_H = 4$ , methyl orange will give a correct result; if  $P_H = 6$ , cochineal will give a correct result; but they cannot *both* give a correct result. It is necessary, therefore, in order to find the best indicator for use in any given titration, to determine the hydrogen ion concentration of a solution of the end product of the titration of the same strength as that produced in the titration. Then if we can find an indicator which has its color change at this hydrogen ion concentration, that indicator (other things being equal) should be the best for use in that titration.

#### TITRATION OF MORPHINE.

The B. P. recommends methyl orange for the titration of morphine; the U. S. P. advises cochineal. In Allen's "Commercial Organic Analysis," Vol. V, page 376, we find: "Morphine forms salts which are perfectly neutral in reaction to litmus and methyl orange, and hence it may be titrated with accuracy by the aid of standard hydrochloric acid and either of these indicators."

Experiments were therefore carried out in order to find the hydrogen ion concentration of pure morphine hydrochloride in 1 per cent. solution, which is about the strength most frequently employed in a titration.

Pure morphine was prepared from ordinary pure morphine hydrochloride by twice crystallizing from a dilute slightly alkaline solution saturated with ether. The crystals were dried and rendered anhydrous by heating at  $115^\circ$ .

$^1P_H$  is the logarithm of the reciprocal of the hydrogen ion concentration in terms of normal, i. e., if  $P_H = 1$  the hydrogen ion concentration is  $N/10$ . If  $P_H = 2$ ,  $N/100$ , etc. The lower the value of  $P_H$  the more acid is the solution and *vice-versa*. At the point of absolute neutrality  $P_H = 7$ .

A solution of exactly N/10 hydrochloric acid was prepared, standardized to phenolphthalein against N/10 sodium hydroxide (free from carbonate), which had been standardized against pure potassium hydrogen phthalate. In one experiment 0.817 gm. anhydrous morphine was dissolved in 28.65 cc. N/10 hydrochloric acid, and made up to 107.5 cc. with neutral distilled water (giving a 1 per cent. solution of morphine hydrochloride). The hydrogen ion concentration of this solution was determined by the colorimetric method, and found to be  $P_H = 3.65$ .

The mean of several experiments gave the  $P_H$  of a 1 per cent. solution of morphine hydrochloride as 3.65. Now, this figure is within the range of the color change of methyl orange, but is on the acid side of the neutral tint, that is to say, a 1 per cent. solution of morphine hydrochloride will give a decidedly pink color with methyl orange. In order to titrate morphine to methyl orange, therefore, we must finish up with a decidedly pink color. As the usual procedure in morphine titrations is to add excess of acid and titrate back with alkali, it is much more likely that the end-point taken will be on the yellow side rather than pink, and the result will be low. But methyl orange is not the best indicator for morphine titrations. If we use brom-phenol blue, an indicator which is yellow in acid solutions and blue in alkaline solutions, we find that a hydrogen ion concentration of  $P_H = 3.65$  corresponds to the first appearance of a distinct blue color when we are passing from acid to alkaline. If, therefore, we dissolve morphine in excess of standard acid and titrate back with standard alkali to brom-phenol blue until a distinct blue color appears we get a more accurate result.

With cochineal, which has a range of hydrogen ion concentration of  $P_H = 5$  to 7, it is obvious that an accurate result cannot be obtained. The results of three titrations with the three indicators may be of interest. In each case the standard solutions were standardized to the indicators used. Methyl orange was taken to its neutral orange tint:

<i>Indicator.</i>	<i>Per Cent. Morphine Found.</i>
Brom-phenol blue	100.0
Methyl orange	99.5
Cochineal	98.8



It may be noted that the statement frequently seen in the textbooks that a solution of morphine hydrochloride is neutral to litmus is unfounded. Pure morphine hydrochloride should be acid to litmus. Two commercial samples of morphine hydrochloride in 1 per cent. solution had a  $P_{H} = 4.83$  and  $4.50$  respectively, showing a slight excess of morphine over hydrochloric acid present. A sample of morphine crystals when titrated to the above end-point gave 101.4 per cent. morphine (hydrated), showing them to be slightly effloresced.

#### THE TITRATION OF QUININE.

Allen's "Commercial Organic Analysis," Vol. V, page 514, states that "Quinine is a strong base, completely neutralizing acids and forming crystallizable salts having a slight alkaline indication to litmus. Quinine also forms a series of acid salts which are neutral to methyl orange."

Squire's "Companion" states that "Quinine hydrochloride is neutral, or at the most but faintly alkaline, in reaction towards litmus paper. It is usually recommended in the textbooks to titrate quinine salts to phenolphthalein. In this way the whole of the quinine is precipitated in the course of the titration, and the end-point is not very satisfactory.

A sample of carefully purified quinine free from other cinchona alkaloids was dehydrated by heating to  $120^{\circ}$ .

0.6744 gm. anhydrous quinine was dissolved in 41.60 cc. N/10 hydrochloric acid, thus forming quinine acid hydrochloride, and diluted to 1 per cent. The  $P_{H}$  of this solution was then determined and found as a mean of three experiments to be 3.40.

Quinine acid hydrochloride should therefore in 1 per cent. solution be neutral to brom-phenol blue, with which it should give a pale greenish-yellow color. Methyl orange would be decidedly pink at this  $P_{H}$ .

0.7144 gm. anhydrous quinine was dissolved in 22.03 cc. N/10 hydrochloric acid and diluted to 1 per cent., forming the neutral hydrochloride. The  $P_{H}$  of this solution was as a mean 5.15.

A solution of this  $P_{H}$  is neutral to methyl red, with which it gives an orange color. It will be seen from the above results that we can most accurately titrate a solution of quinine hydrochloride or sulphate by adding standard acid until a pale greenish-yellow color corresponding to  $P_{H} = 3.4$  is obtained. A commercial sample of

quinine hydrochloride titrated in this way gave 99.79 per cent. In the same way quinine acid hydrochloride or sulphate may be titrated with standard alkali until an orange color corresponding to a PH of about 5.15 is obtained with methyl red solution. A sample of quinine acid hydrochloride titrated in this way gave 97.3 per cent. The end points are not quite so sharp with quinine as with morphine, but with a little practice quite reliable results can be obtained. This method of titration may be applied to tinct. quinin. ammon. for the combined determination of quinine and ammonia in the following manner:—25 cc. of the tincture are run into 50 cc. N/2 hydrochloric acid, brom-phenol blue is added, and the liquid titrated back with N/2 alkali until a pale greenish-yellow color is obtained. Let  $a$  = No. of cc. N/2 alkali used. Methyl red is then added to the solution and the titration continued with N/10 alkali until the pink color of the methyl red disappears and only the blue color of the brom-phenol blue remains.

Let  $b$  = No. of cc. N/10 alkali used.

$$W/v \text{ quinine sulphate B. P.} = b \times 0.1763.$$

$$W/v \text{ ammonia} = 50 - \left(a + \frac{b}{5}\right) \times 0.034.$$

Commercial samples of quinine salts tested in 1 per cent. solution gave the following values for PH:

	<i>Ph.</i>
Quinine hydrochloride	6.2
Quinine acid hydrochloride	3.7
Quinine acid sulphate	3.6

#### THE TITRATION OF ATROPINE.

The B. P. and U. S. P. employ cochineal for the titration of the alkaloids obtained from belladonna.

Squire's "Companion" (nineteenth edition) states that "atropine may be readily determined by titration, using cochineal or iodeosin as an indicator." Atropine sulphate is stated to be neutral to litmus paper.

Allen's "Commercial Organic Analysis," Vol. V, page 296, states that commercial atropine sulphate is often faintly alkaline, and keeps better when so made.

In order to determine the PH of a 1 per cent. solution of atropine hydrochloride, a known weight of pure atropine was dissolved

in the theoretical volume of N/10 hydrochloric acid and made up to 1 per cent. strength. The  $P_{H}$  of the solution was found to be 3.75.

This corresponds to a distinct blue color with brom-phenol blue, and is reasonably close to the end-point of the morphine titration given above. It is again evident the cochineal is an unsuitable indicator for this titration, and that brom-phenol blue should be used, finishing with a distinct blue color.

A commercial sample of atropine sulphate had in 1 per cent. solution  $P_{H} = 5.9$ , showing that it contained an excess of atropine over the sulphuric acid.

#### SUMMARY.

On theoretical grounds and as the result of practical experiments it has been shown that the indicators ordinarily employed for the titration of the alkaloids, morphine, quinine, and atropine, are not the most suitable for the titrations.

From measurement of the hydrogen ion concentration of the solutions of the pure hydrochlorides it was found that brom-phenol blue is a better indicator to use for morphine, atropine, and the neutral salts of quinine. For the acid salts of quinine, methyl red is the most suitable indicator.

The work for this paper was carried out in the analytical and research laboratories of Messrs. Allen and Hanburys, Ltd.

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### THE POLLUTION OF WATER.\*

At the meeting of the American Public Health Association in San Francisco, an experienced biologist made the startling statement that if present conditions continue, the greater part of the eastern United States will be cradled in a septic tank.<sup>1</sup> The growing sewage pollution of our rivers and seashore has long been recognized as a problem of serious moment. There is one aspect of the subject, however, that is not generally understood. House sewage, which represents human wastes, may, of course, contain the micro-

\*From *Jour. Amer. Med. Asso.*, July 30, 1921.

<sup>1</sup> Nelson, T. C.: Some Aspects of Pollution as Affecting Oyster Propagation, *Am. J. Pub. Health* 9:498 (June) 1921.

organisms of infectious disease and thus represent a potential menace to those who drink water or eat food that have been contaminated by it. But domestic sewage ordinarily contains nothing detrimental to the growth of the aquatic organisms which help to complete the disintegration of the excreta and which thrive on it. Sewage, indeed, supplies a source of plant and animal nutriment in the water as truly as on the soil. Nelson reminds us that under favorable conditions a small stream may dispose of the sewage of a relatively large population, and the stream in turn be supplied with a constant source of animal and plant nutriment. There is a true fertilizing action on the water, with a resultant large increase in the number of the organisms present. Since fish and shellfish utilize these plant and animal organisms as food, it follows that the addition of domestic sewage to a body of water will result ultimately in an increase in the amount of human food, in the form of fish and shellfish derived from it, as truly as though the sewage were employed in fertilizing land crops. The danger of eating shellfish removed from grossly polluted water thus lies in the presence of pathogenic bacteria, rather than in the inert organic matter present in the medium. The problem of purification of such products as oysters primarily becomes one of sanitary bacteriology. It can be met by avoiding the pollutions; or, if this is not entirely feasible, the food can still be conserved by disinfection procedures. But of late the oyster itself is becoming threatened with extinction because of an added kind of contamination represented by the great industries which discharge effluents into the streams reaching the coast. Oils, acids and alkalis, metallic poisons and other chemical compounds may interfere with all forms of life, whether micro-organisms which themselves aid in the self-purification of our natural waters, or the animals and plants which normally thrive and develop in them. In other words, the disposal of industrial wastes has complicated the disposal of human waste, and incidentally an important source of delectable human food is likely to be impaired. Something remedial must be done, and soon.

## NEWS ITEMS AND PERSONAL NOTES

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DR. ALSBERG RETIRES FROM U. S. BUREAU OF CHEMISTRY.—Dr. Carl L. Alsberg, who has been Chief of the Bureau of Chemistry of the U. S. Department of Agriculture since 1912, has retired from that office.

He has attached himself to the Ford Research Institute of Stanford University, California, where, with other investigators working along associated lines, problems in Ford Chemistry and Nutrition will be worked out.

His place in the Bureau of Chemistry will be temporarily filled, at least, by Walter G. Campbell, who has been appointed Acting Chief. Mr. Campbell has been closely associated with the work of the Bureau since 1907, and for some time has been Assistant Chief under Dr. Alsberg.

Dr. W. W. Skinner, Chief of the Water and Beverage Laboratory since 1908, has been named Assistant Chief of the Bureau.

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## BOOK REVIEWS

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"BULLETIN OF THE NEW YORK BOTANICAL GARDEN." By H. H. RUSBY. 2:1-318. April, 1921.

This volume is a guide to the Economic Museum of the New York Botanical Garden, which has been established to furnish illustrations of useful plant products, and wherever possible, choice specimens of the plant yielding them. Dr. Rusby points out in the introduction that to a large extent, the collection represents aboriginal as well as domestic customs and uses, that the articles exhibited have positive authentication, and that at great labor and expense large amounts of material preserved for the most part in formaldehyde solutions are present in the museum for study and observation. The museum now contains 8000 articles.

It has been found convenient to group the articles in relation to their use as products, and then to subdivide these larger divisions either in the evolutionary sequence of the plants yielding them, or as in the case of foods and drugs from root to seed.

The rest of the bulletin is taken up by a comprehensive catalogue of exhibits with clear descriptive notes.

M. S. DUNN.

# THE AMERICAN JOURNAL OF PHARMACY

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## EDITORIAL

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### THE AMERICAN SYNTHETIC CHEMICAL INDUSTRY.

Born of necessity, reared with much difficulty, and just reaching the stage where its knees were strong enough to sustain it, the infant American Synthetic Chemical Industry is threatened with an affliction which may lead to its early demise. It needs no learned prognostician or diagnostician to point out the nature of the oncoming ailment or to realize that quick means need be taken to fortify the patient against the attack.

Before the onset of the great World War there had been poured over this country a vast avalanche of tar synthetics, most of them designed to become permanent elements in the physicians' *armamentaria* for fighting disease. Many of them possessed distinct merit, and had created for themselves an unquenchable demand. The majority of them, however, were foisted upon the credulous doctor, for the good doctor has well earned this title, and for all practical purposes were merely makeshifts and only valuable as providing means for the astute German to unload some valueless by-products of tar for which his chemist could find no other avenue of sale.

It is said upon good authority that "once upon a time" a certain German firm found itself hampered with a fairly large consignment of a crystalline coal tar compound for which it could find no earthly use. A clear-visioned and not too scrupulous chemist, knowing that the compound was relatively harmless, advised packaging the article in 10 gramme units, assigning to it a sonorous chemico-therapeutic name and sending it over the seas to cure American migraines. Accordingly so was it done and the firm was promptly

cleaned out of its encumbrance and relieved of all worry as to the disposition of any such future accumulation of worthless by-product.

We are not enthusiastic about the correctness of the foregoing premise, but correct or not, it most certainly carries the message with it that America was a profitable dumping ground for an endless array of worthless therapeutic agents of this type, whose vogue ran parallel with the extensiveness and intensiveness of their advertising and soliciting campaigns.

The war, however, closed the ways to all of these synthetics, good and spurious alike, and America, who had given the Germans and others an unopposed right of way in the manufacture and exploitation of such remedies found itself denied of many articles of real therapeutic merit. So great had been our dependence and so complete our indifference that during the early part of the war such common substances as acetphenetidin, antipyrin, resorcinol, acetanilid and hydroquinone were marketed at ridiculously high prices and much distress was occasioned through the scarcity of other products of marked remedial value, such as arsphenamine and diethylbarbituric acid. American enterprise soon found a way out, however, and both in the matter of synthetic drugs and dyes quickly approached a season when independence of Germany was an assured fact. Quite naturally our joining in the fray made more insistent demands upon our industries and particularly upon the chemical industry which bore the burden of the work of supplying the high explosives and warfare gases. Indeed so great was this demand that the infant synthetic chemical industry quickly grew to a healthy condition. Augmented by those other factors the drug supply soon became large enough to supply the demand and prices reached a scale lower than ever before, particularly the prices of many of the synthetic patented drug products, the sale of which had previously been a German monopoly.

It is granted, of course, that the infant industry waxed strong and hearty in the absence of active competition. Now, however, the ratification of peace with Germany, where most of these synthetics had their origin finds that country making ready to bid again for a market for both their good and bad products.

This is where our infant industry may find its agent of destruction unless the antitoxin of encouragement be used to combat this factor. This country should undoubtedly provide for the manufac-



ture at home of all of the worth-while remedies and means should be found, despite foreign propaganda, to protect this industry in every possible manner.

Physicians should be on their guard against vicious and guileful propaganda directed against American products and pharmacists should insist upon buying and using American-made synthetics whenever possible.

Proof positive of the assembling of arms for an active campaign to re-establish the sale of German-made products is seen in the following paragraph taken from the *Munchener Medizinische Wochenschrift*, August 26, 1921 (through *Jour. Amer. Med. Assoc.*):

"The firm of E. Merck (Darmstadt) has had a unique film prepared which gives a survey of its various forms of activity. It is to be used in advertising in foreign countries the German chemical and pharmaceutical industry. Excellent pictures are produced not only of the buildings of the extensive plant, but also of scenes in the various factories and machine shops. Beginning with the raw material and leading up to the finished product ready for shipment, the manufacture of the most important drugs is shown; also the methods of producing therapeutic serums, with a glimpse at the enclosure in which the animals needed are kept. The onlooker gets also an insight into the work of the mercantile departments. Before the film should start on its world journey, it was shown in Darmstadt, August 14, to a circle of invited guests. The very interesting production, which consists of five parts, required an hour and a half for its exhibition, without oral demonstration."

Here is food for thought and reasons for this editorial message.

I. G.

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## ORIGINAL PAPERS

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ADDRESS OF FRANCIS P. GARVAN,\*

PRESIDENT OF THE CHEMICAL FOUNDATION.

That the cause and the chief lesson of the World War was most truly appreciated by Pasteur when he said: "Science is the soul of the prosperity of nations and the living source of all progress—what really leads us forward are a few scientific discoveries

\*Delivered before the joint session of the Society of Chemical Industry and American Chemical Society, at Columbia University, September 7, 1921.

and their application," was pointed out by Francis P. Garvan, President of the Chemical Foundation, who appealed to the chemists of this country to accept the responsibility for teaching the people of this country this truth as applied to the critical chemical situation of the nation.

"The people of the United States are ninety-nine per cent. right at heart and appreciative," he declared. "So are the people of England and of Canada. Their appreciation of chemistry must no longer be deferred in the terminology of the propaganda of foreign hostile interests, seeking only their destruction. Your work must never again be allowed to cease in the laboratory."

After describing the discovery by the English chemist, Perkin, of the basis for the subsequent development of the coal-tar industry and practically all organic chemistry, Mr. Garvan told how "the German, Hoffman, put this discovery in his bag and took it back to Germany," where "almost instantly he was able to make German industry, German universities and the German Government realize the importance of that bag."

"Immediate success led to a greater appreciation of an ever closer alliance of science and industry and an ever closer alliance between science, industry and the militaristic state," he declared. "This triple alliance changed Germany from an agricultural nation into the second industrial nation of the world, but in that change, it brought about a succession of periods of over-production, each one in turn overcome by greater consolidation, by ever increasing corruption in methods of bribery, espionage, dumping, *et cetera*, and by ever intensified state aid and direction. In 1914, we find the German people demanding the control of the markets of the world. We find their hearts corrupted by the methods which they had felt it necessary to adopt to overcome their successive periods of over-production. We find them swollen with pride at their successes and ready to inspire or acquiesce in the hazard of battle. This triple alliance of industry, science and the militaristic state—and the evidence is overwhelming that each was equally guilty—considered that it would be quicker and cheaper to attempt to gain this end by victory on the field of battle, rather than to find increased markets for a surplus production by further intensified methods of peaceful penetration.

"The same chemical research with its well-served industry had

in turn well served the militaristic state. As chemical progress indexed commercial progress, so explosives had kept pace with dyes and pharmaceuticals, the ammunition factories of her peaceful penetration were the arsenals of her munitions preparation.

"In the fall of 1913, the chemical application of Perkin's discovery was able to notify the war lord that Germany was ready; that she controlled 95 per cent. of the organic chemistry of the world, upon which industry and the production of war gases and explosives were dependent; that she had crushed out every incipient effort toward the development of the Perkin discoveries by every other nation and was able to deal the dependent industries of those nations tremendous blows, and that now by the final triumph in the development of the Haber processes of making nitrates from the air, her agricultural production and munition production were safe from the menace of any blockade. You know the rest.

"All this German chemists accomplished not alone in their laboratories, but in the forum of public opinion. They had educated and moulded thought in Germany until every man of whatever rank, in or out of industry, education or governmental service, realized the importance of chemistry in his life and in the life of his country. They knew that the alliance of science and industry had increased the wealth of the world a thousandfold in the past hundred years. They knew that it was the life blood of industry; they knew it was the safety of their state and the only sure foundation upon which to base the hope of the health of their children's children, and they had impressed upon the world the discouraging and withering idea that the Germans and the Germans alone were mentally equipped to lead in this great age of chemistry."

As an instance of the foresight of German chemical interests, Mr. Garvan told how "prior to 1908 German patent laws contained the so-called working clause, by which your inventions, if patented in Germany, must be worked there within a certain period of time or they were thrown open to the German manufacturers and developers. Agitation was rife in this country that we should protect our future in like manner. But by 1908, Germany had decided that she had so far advanced in science that she no longer needed that clause to protect herself and that if enacted by the United States, it would threaten her control of organic chemistry in the world and destroy the purposes upon which she was bent.

"The President of the Bayer Chemical Company, at that time the head representative of this march for world control in America, although on paper an American citizen, acting under instructions from the consolidated government and chemical industries of Berlin, went to Commissioner Moore at the Patent Office in Washington. It was the beginning of one of Washington's hot summers. With fulsome praise of his outstanding position in the patent world and the great inventive genius of this country needing protection, he reproached him for not representing the United States at the International Patent Conference about to be held in Stockholm. Mr. Moore responded that the unenlightened Congress had not given him any funds with which to go. Mr. Moore then went on his vacation. Mr. Muurling, the predecessor of Schweitzer and Metz as the American voice of Germany's chemical interests, went to Robert Bacon, then acting Secretary of State, drew the picture of the United States unrepresented at that great conference, pointed out to him that he had a fund which he could apply to any purpose which he deemed for the best interests of the country in its foreign relations, with the result that Mr. Moore was recalled from his vacation and sent abroad, but with him went a letter to the German chemists, telling them that the American representative of the German dream had done his part and that they must now do theirs.

"The result was that Moore was induced to go from Stockholm to Berlin, where he was feted and dined by the Kaiser himself and returned to negotiate the treaty of 1909 with Germany, by which Germany was released from ever working her chemical patents in this country and by which the last hope of development of organic chemistry in this country was crushed. No more loyal Americans ever lived than Robert Bacon and Commissioner Moore, but they were unconscious tools in the hands of the German chemists, the handmaidens of the German dream of world control. And you were to blame because you had not instructed your government officials up to a realization of the importance of chemistry and its guidance and protection by the State."

"In Germany today industrial reorganization for world domination first in the peaceful arts and then in war is proceeding mightily under the sympathetic eye and fostering care of a government which differs in no important particular, so far as the world outside of Germany is concerned, from the government of the Hohenzollerns,"

said Mr. Garvan. "The German purpose stands forth as clearly as a mountain in the sunlight. First, reconquer in industry and commerce, then we Germans will see. Their secret documents prove it. The heart of the news that comes out of Germany proves it. They prove it out of their own mouths.

"Moles in the darkness, German agents in America are once more plotting against our security, our prosperity and against the health of our very children. The German design to render the United States important is being prosecuted today with more subtle viciousness than marked the intrigue of Von Bernstorff, Dr. Albert and Hugo Schweitzer in the years before we entered the war.

"The times are too tense with danger for passive tactics. On one side we have the same old crowd of German agents masquerading as good Americans. On another side we perceive American citizens supporting the German intrigues. In Congress we hear and stand aghast at the ignorant and malicious outburst of certain legislators, unmindful of their country's welfare. Folly drips from their mouths. Stupid suspicion of the motives of honest men and appalling ignorance of the times mark their astounding incapacity. There are some, who, like Jacob of old, have set themselves to steal the birthright of chemical independence from the American nation. They may disguise for a time the hairy hands of the German dye monopoly that controls them, but in the end the people will know them for what they are. Their voices are the voices of elected Representatives and Senators in the American Congress, but the hands that manipulate them are the hands of the German dye trust, the most powerful monopoly ever formed by man, the *Interessen Gemeinschaft*, the 'I. G.'

"If, in the reaction of war and in the general distaste for discussing matters pertaining to war, we permit ourselves again to be lulled and numbed by German propaganda, if we look on indifferently while a few demagogues in Congress and a few short-sighted, selfish men in business life play the German game, if we allow Germany to stifle an American industry that would within a very few years make the United State absolutely safe, then, I say, it will have been through your neglect and temerity and failure to realize that it is your responsibility not only to search the truth, but to preach it.

"Your responsibility today is the same as it was during all these

years, of neglect, only intensified as it must be by your consciousness of the results of that neglect. You have listened without apparent protest contenting yourselves with resolutions and telegrams to swell the waste paper baskets of Congress, to the German lie that there was a 'Dye Monopoly' in this country, or that such a monopoly would result from the enactment of a selective embargo, when you knew that the development of a dye industry is synonymous with the development of education in organic chemistry and that no monopoly in education is possible without the compulsory partnership of industry, university and government, such as exists in Germany. (A monopoly which never worries those tools of German propaganda.)

"Did it not bring in your minds the lessons of the war when you saw the importing representative of the German 'I. G.' stand on the floor of the House of Representatives, flanked by fifteen of the seventeen Congressmen who voted against the declaration of war, leading the cheering when the first great unsuccessful test came as to whether American chemists should be given a chance to catch up their neglect of forty years and atone for it by leading this country through the development of organic chemistry into the realms of intensified national industrial progress, secret security to home and child and blessed advance in the medical service of humanity? Do you not feel that the voices of two German importing firms were louder in protest and more persistent in their appeal for Germany than the voices of your fifteen thousand members for America's lessons of the war?

"Again I repeat, Herman A. Metz stood upon the floor of the House as that vote was announced and shouted to a gallery of American citizens, 'I've got you licked.' And when he screamed in triumph, he meant 'I, the representative of the Interessen Gemeinschaft, the 'I. G.,' the combination of German government and German chemical industries; I've licked the advice of your General Pershing; I've licked the advice of your Secretary of War; I've licked the advice of your Secretary of Navy; I've licked your President; I've licked your Administration; I've licked your thirty million dollar investment in your colleges; I've licked your chemistry in your high schools and your public schools; I've licked your research institutions and the future development of medicine in America.'"

After outlining the development of the peace idea and the progress of war weapons up to the discovery of war gases, Mr. Garvan said:

"These things hit at the heart of imagination, surveying what creative chemistry has already done in war in its first few experimental steps, we stand back impressed as never before in the whole history of war tools. We are bound by sheer intelligence to comprehend that chemical science 'has only begun to fight.' It has learned how to utilize, not very skillfully, a few gases. It has not done anything beyond small scale experimenting with radio active forces. But the lessons of the great war were a tremendous impulse to the research chemist. The creative chemist is searching out among rare elements, such as radium, arguments against warfare that can no more be refuted than pigmy man can oppose the tornado, or the earthquake, or contend with Vesuvius. The strange stuff that illuminates the dials of our watches may be the very medium that will eventually produce the resistless force that will make fighting intolerable.

"Chemists are seeking through forces as yet imperfectly comprehended to turn man toward sanity. They are, aiming at his imagination. Who will dare say they are pursuing a fruitless quest after the experience of the great war which began as a war of great steel projectiles and ended as a war of invisible energy. Hard-headed military men, usually slow to convince that weapons other than the traditional arms of their service must be learned and relied upon, join nowadays with chemists in an appeal to the public understanding which is little short of the striking appeal made by the imaginative story of Mr. Wells, for they realize that chemistry is merely on the brink of great things, and none see so clearly as they that chemistry aims to abolish war by making it desperately perilous to great nations as well as small, to governments as well as to the led peoples; to vainglorious politicians as well as to the obedient servants in uniform."

Following a description of Dr. Hugo Schweitzer, as a chemist, scientist and researcher, a German spy, secret service number 963,192,637, head of the German Secret Service in America, head of the system by which every effort to develop the organic chemical industry in this country was crushed out, head of the system of dye

salesmen by which every fact and circumstance of the four billion dollars a year American dependent industries was reported to Berlin, carded and charted there, taken into the great industrial establishment at Grosser Lichterfeld, outside of Berlin, and there placed at the disposal of competing German industry; the inventor of the idea of the purchase of the *New York Evening Mail* to corrupt our information; the inventor of the idea of the German Publication Society, formed to publish for our delectation the literature of German Kultur; head of the chemical exchange, by which all available phenol supply in America was turned away or made inaccessible to the Allies," Mr. Garvan concluded:

"Gentlemen, personal responsibility is a thing that cannot be escaped. We may go to our graves, but there will come forth from the unforsecable transmutations of destiny or from the divine will, some reaction of our unconsidered acts or of our deliberate evasion of the moral law that may cause misery to a multitude.

"Two years ago there leaned against a lamp-post on the Bowery, a strange Jew, with only his landlady's borrowed quarter in his pocket, only hate in his heart and wrong-thinking in his head. To-day this man, Trotzky, controls the destinies and happiness of three hundred millions of Russian men, women and children. He, the mouthpiece of false ideas seized upon the ignorant and desperate mass in the hour of their agony, and has proved their destruction. Contrast his unwholesome and blasphemous career with that of Joan of Arc, who has always seemed so human, so natural, so close to all of us, her sweet, simple, girlish figure, sublime in her faith, sustained in her virtue and mighty in the power of her dominant will and the justice of her cause. She has been with us now for hundreds of years and never more so than during this war when she staunched the heart of France and led her brave as of old. As it is with these two individuals of humble origin, so it is with the highest. Contrast the Emperor of Germany, in whom self-love and ambition had crushed out all spirituality, leading his people and forcing them on in the conquest which has brought such unspeakable misery and suffering to untold millions of men, women and children—contrast him, I say, with that magnificent figure, Cardinal Mercier, that soul of resistance to injustice and falsehood, whose memory constitutes a solace, stored up for the distressed people of all future times.



"As it is with the lowly peasant man or woman, as it is with the emperor on his throne, or a prince of the Church, so it is with the scientist or the researcher. Contrast the influences intended by Perkins, who, at the end of his life, received his richly earned honors with bowed head and in humble voice: 'What is it that I have not received? Not unto me, O Lord, not unto me, but unto thy great name be all the praise.'

"Contrast him, I say with Schweitzer, the scientist and researcher, representative of the profane application of his science in peace and war, and in the shadow of that contrast, and in the humility and in the shame which we should feel, let us look forward to the day when the English and American chemists can meet again, with the evidence about us of our atonement for our neglect, evidence of permanent peace in all the world, of a higher and more equal standard of living for all our peoples and of a great marching forward in our battle against disease. Until that day let no man write his epitaph."

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## METHYL-ORANGE AS AN INDICATOR IN PRESENCE OF INDIGO-CARMINE.\*

By PROFESSOR FRANK N. MOERK.

Methyl-orange used with the more dilute or weaker volumetric solutions for accurate work should be compared with a blank test to correct for its alkalinity and also to reduce error because of the gradual color change.

In a pamphlet issued in 1914 by the Wilckes, Martin Wilckes Company, of New York, on "Methods for determining the strength and impurities in Acid Calcium Phosphate" a formula is given for preparing an indicator for the "determination of free phosphoric acid" by the use of which the change in color is more sharply distinguished; 25 cc. of a solution of Methyl-orange (1:1000) are mixed with 5 cc. of water containing 0.09 Gm. of sodium sulph-indigotate (indigo-carmine).

Looking up the literature of this mixture as an indicator, *Chem. Abstr.* 1908, page 165, gives reference to an article published by R. Luther in *Chem. Ztg.*, 1907, page 1172, in which priority for the

\*Read before meeting of Pennsylvania Pharm. Asso. June, 1921.

\*Chemical Laboratory Philadelphia College of Pharmacy and Science. June 10, 1921.

combination was claimed quoting an article by J. A. Af Hällström in *Berichte*, 1905, page 2288.

The several original articles in the order of their publication contain the following information:

(1) J. A. Af Hällström in an investigation found it necessary to determine alkaline carbonates and bicarbonates in presence of phloroglucin; as the solutions were always colored, the titration with HCl V. S. (ethyl-orange indicator) was unsatisfactory. Prof. R. Luther, under whose direction the investigation was made, suggested the addition of indigo and this then enabled more satisfactory titrations.

(2) C. Kirschnick in *Chem. Ztg.*, 1907, page 960, published an article under the title of "Indicator for the determination of free acid in zinc chloride solutions, etc." The demand for an indicator which combined the sensitiveness of methyl-orange with a better end-reaction in turbid or light-colored solutions induced the author to bring about a change in color of the methyl-orange solution. It was found that an addition of indigo-carmin under certain conditions of dilution produced a pure green color which by the minutest addition of normal acid changed to a violet-red. The following dilution proved practical: One gram of methyl-orange and one gram of indigo-carmin were each dissolved in one liter of water; 20 cc. of the methyl-orange and 60 cc. of the indigo-carmin solutions were mixed and diluted to one liter.

This mixed indicator was used in testing zinc chloride in the following manner: 10 cc. of the indicator was diluted with 100 cc. of water and 10 cc. of the zinc chloride solution (25% Zn) added; an unchanged green color shows basicity, a resulting red color shows acidity of the zinc chloride; by titration, the basicity or acidity of the salt can be determined. This indicator can also be used to determine the free acid in superphosphate. Pure indigotin dissolved in sulphuric acid and carefully neutralized can replace the indigo-carmin.

(3) B. Luther in *Chem. Ztg.*, 1907, page 1172, furnishes more information under the title of "On the addition of Indigo in titrating with methyl- or ethyl-orange."

"In the *Chem. Ztg.* 1907, page 960, C. Kirschnick recommends an addition of indigo in titrating yellow colored solutions with

methyl-orange. Two years ago J. A. Af Hällström upon my suggestion applied the same addition for the same purpose. As the intended detailed publication of this artifice was postponed until the completion of some additional experiments, a few statements may be communicated at this time.

"The addition of indigo to yellow colored solutions undoubtedly increases the sharpness of the end-reaction. But we must not forget that the quantity of indigo-carmin to be added must be proportional to the yellow coloration. The more intense the yellow color the sooner will appear the change of color from violet to green and so much later the change from green to violet. A definite formula for the mixture suitable for all degrees of yellow colorations is not possible. In case of approximately uniform yellow color solutions and, especially, in cases of somewhat concentrated solutions for titrations this condition need hardly be considered, as the addition of indigo-carmin allows titration which would otherwise be impossible.

"It appears to me that the addition of indigo-carmin in the accurate titration of colorless solutions with methyl- or ethyl-orange is of even greater value than in the titration of yellow colored solutions.

"To obtain distinct end-reactions in titrations with alkaline hydroxides containing carbonate the suggestion of Küster is followed by preparing a 'normal color' by saturating the methyl-orange solution with carbon dioxide and titrating to this color. As the changes in color, red, orange, yellow, especially in dilute solutions, are gradual the end-reaction may be doubtful. In these cases indigo-carmin is of advantage as its color is practically complementary to the 'normal color.'

"It is possible by a few trials to obtain the proper mixture of methyl-orange and indigo-carmin which will result in giving an almost neutral gray with carbon dioxide; sufficiently dilute solutions of such a mixture will then appear almost colorless.

"The change in color from violet, though colorless, to green is very pronounced and titrations in dilute solutions, especially, are more easily made; the end-reaction is colorless (gray.)

"As indigo-carmin with excess of alkali changes to yellow, the complete color changes obtainable in titrating an alkali with acid is as follows: yellow, green, colorless (gray), violet. The multiplicity of color changes has the advantage of preparing one for the approach of the end-point; overstepping the end is therefore, even in rapid work, easily avoided.

"Very few references in literature were found mentioning the yellow color produced by dilute alkalies on indigo derivatives."

The two formulas given above if calculated to a common basis will not agree; several other mixtures were made:

	<i>Methyl Orange.</i>	<i>Indigo Carmin.</i>	<i>Water.</i>
A	1.000 Gm.	3.6 Gm.	1000 Cc.
B	1.333 Gm.	4.0 Gm.	1000 Cc.
C	1.000 Gm.	2.5 Gm.	1000 Cc.
D (Kirschnick)	1.000 Gm.	3.0 Gm.	1000 Cc.
Wilkes	0.833 Gm.	3.0 Gm.	1000 Cc.

0.2 cc. of D diluted to 100 cc. will duplicate the strength recommended by Kirschnick. The first four solutions (C and D preferentially) were used for experimental purposes and were found to give uniform results in titrations with tenth-normal volumetric solutions if the following details were observed:

Dilute two portions of 0.2 cc. indicator with 100 cc. of water and add to the green or greenish-yellow solutions just enough acid volumetric solution to discharge the yellow or green color without producing a red or violet color; should the latter color show add enough alkali to discharge it. The object is to produce a "neutral tint" showing neither alkalinity nor acidity; disregard the volumetric solutions necessary to accomplish this.

Reserve one of these solutions and to the other add the substance to be titrated; a violet or purplish color indicates an acid substance, a yellow or green color indicates an alkaline substance. Titrate with an alkali or an acid volumetric solution, as the case may require, until the color matches that of the reserved solution. It is next possible to add to the reserved solution another portion of the substance to be titrated and check this against the previously titrated portion. The titrated solution will respond by color change with a single drop of acid or alkali volumetric solution.

A modification of this method was tried by taking in duplicate, 10 cc. water, 0.05 cc. indicator, then traces of acid volumetric solution to yield the neutral tint (which in this case is colorless); next add to one of the solutions the substance to be determined and titrate with acid or alkali volumetric solution to reproduce the neutral tint. As only a few titrations were made by this modification, preference is given to the first method.

The following substances were titrated in the course of the above work: Sulphuric and phosphoric acids, sodium borate, carbon-

ate, hydroxide and phosphate. It should not be necessary to here state that the standardization of the volumetric solutions employed must be made by the same method.

Solutions are submitted to show changes in color of methyl-orange in comparison with the mixed indicators A and C, these illustrating the greatest variation in the quantities of methyl-orange and indigo-carmin.

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## EGYPTIAN SECRETS AND MAGICAL SPIRIT ART OF THE PAST AGES.\*

By EDWARD J. HUGHES, P. D.

The practice of witch-craft, the white and black art, voodooism, or hex-doctoring is considered by most people, in our enlightened age, as a reflection upon our intelligence. Yet it is surprising to find that only a few hundred years ago the treasured Egyptian secrets were highly esteemed and the magical spirit art was practiced by men of highest repute, such as priests, alchemists and philosophers. Then too, we are reminded by the newspapers that in our present day there are those who seek to find relief from their sufferings and confusion by the use of charms and incantations.

Needless to say, it is not the object of the writer to advocate the use of these weird hallucinations. Nevertheless it is interesting as well as amusing to examine some of the ancient literature and there find recorded the cure-alls that were in vogue at that time. Signed statements are made, apparently with sincere reverence, as to the efficacy of these remedies, and miracles are said to have been wrought by methods which to us may seem ridiculous.

One of the books dealing with the magical spirit art is called the Sixth and Seventh Book of Moses. The copy of this in English is said to have been translated from the German and that, in turn, from the ancient Hebrew. This contains a mass of incoherent material showing about as much connection throughout the text as one might expect to find in an ancient dictionary. It contains a lot of hieroglyphics, symbols, seals, magical formulas and incantations. Besides these it contains a collection of writings from both the old and new Testaments with many other sacred writings of doubtful

\*Read at the Convention of the Pennsylvania Pharmaceutical Association, held in Philadelphia, Pa., in June of 1921.

authority. It is distinctly a book of faith cures. The last few pages of the book are devoted to astrological influences upon man and the magical cures of the old Hebrews. Among the latter are the following examples:

Diseases of the Eye:—The saliva of the first-born on the male side (not of the female side) is effective in the cure of eye diseases.

Fever:—Take a seat on a cross-road and as soon as you observe a large ant carrying something, take her up and place her in a copper tube. Close the opening with lead and seal it with sixty seals, shake the tube and hang upon your body and say to the ant: Thy burden upon me and my burden upon thee.

Another literary curiosity is found in the book of *Egyptian Secrets* by Albertus Magnus, revealing the forbidden knowledge and mysteries of the ancient philosophers. The statement is made in the preface that this book was issued for the purpose of rendering a great service to mankind and in order to bridle and check the doings of the devil. It is also claimed, by Albertus Magnus, that these secrets have been proven and found efficacious by those having the true belief.

The following list of examples taken from this volume gives a fair conception as to the nature of its contents:

For Bad Hearing. Take the oil with which the bells of churches are greased and smear it behind the afflicted ears and relief will not fail to come at once.

To Make Ones Self Invisible. You must obtain the ear of a black cat, boil it in the milk of a black cow, then make a thumb cover of it and wear it on the thumb and no one will be able to see you.

How To Be Able To See In The Darkest Night. Grease the eyes with the blood of a bat.

To Ascertain Whether A Sick Person Will Become Well Again. Cut a piece of bread, rub the patients teeth therewith, and throw it before a dog. If the dog eats it the patient will recover. Otherwise the disease is dangerous.

To Facilitate Healthy Sleep. Procure two rabbit ears, place them under the pillow of a person who cannot sleep, without his knowledge.

To Drive The Mice Away From Barns. Burn a rotten crab to powder, fumigate the barns with it and all the mice therein will die.

To Make The Hair Grow Wherever You Choose. Take dog's milk and paint the spot therewith wherever you wish to have the hair grow. It will surely grow.

To Make a Person Dislike Gambling. Speak to an executioner, give me some wood of a whip wherewith you have beaten criminals and flog the gambler with this upon his naked body. Nevermore thereafter will he gamble.

To Catch Fish. Take valerian or cocculus indicus and make small cakes thereof with flour, throw these into the deep. As soon as a fish eats thereof it will become intoxicated and float upon the surface.

When You Hear Something Said That You May Not Forget It. Take the heart of a swallow, boil it in milk, and carry it on your person and you will remember all you hear.

The selection of the foregoing list is not designed to discredit the accomplishments of Albertus Magnus. History records him as one of the foremost of the medieval philosophers. He was known as the Universal Doctor in addition to being an astronomer, a theologian and an alchemist and knew practically all that was to be known in his time.

Not all of the secrets published by Albertus Magnus in this volume are of the same superstitious and somewhat magical character. Some of the remedies employed by him have passed safely through the centuries and are valued pharmaceutical substances and medicinal agents of the present day.

For instance, a splendid eye water is recommended composed of white vitriol, native camphor and rose water. Constipated persons are told how to open the bowels within one hours' time by taking a dose of salts and senna such as apothecaries sell. The value of astringents in stopping the flow of blood is utilized in a remedy for nose bleeding which directs that a little wadding be dipped in good ink and inserted into the nose or other bleeding injuries. An ointment for burns is recommended containing rosin, tallow, wagon grease, wax and turpentine oil. A blister plaster is found composed of cantharides, turpentine, yellow bees-wax and linseed oil. Another ointment for burns is directed to be made by mixing upon a coal fire two ounces of turpentine, three ounces of yellow bees-wax and six ounces of linseed oil.

For a time alchemy was associated with superstition in the hands of magicians and practitioners of the black art. We are told,

however, that the quackery and mysticism that did much to discredit alchemy during its later period were the products of an ignorant and superstitious age and the result of the inability to read and understand some of the ancient manuscripts.

The recent revelations of the extent to which the charms, incantations and queer ceremonies of witch-craft still flourish in some of the rural sections of Pennsylvania bears evidence that even today many people are following along the lines of ignorance and superstition and are calling upon the witch doctor for relief.

In one instance two verdicts, aggregating \$15,000 in damages, were awarded to the father of two girls over which the witch doctor had acquired almost absolute control. On one occasion he bored a hole in a tree with an auger, clipped off the girls' hair and placed it in the hole, meantime mumbling mystic words.

The newspapers reported a case only a short distance from Allentown, Pa., where a man and his wife were shot because the would-be murderer believed that they had bewitched him.

Another interesting news item was to the effect that a witch doctor had been arrested in Reading, Pa., for having obtained money under false pretense. This was said to have caused a fine flutter among the best people of Berks County who feared that he might betray some of their family secrets.

The most fertile soil for the development of a belief in the efficacy of the black art, magical spirit art, quack doctors, witch doctors or any other form of pow-wow is found in the mind of the ignorant and uneducated. Like the people of the dark ages their tendency seems to be to look to the supernatural, the magical and the mystifying. They are not acquainted with the facts so their efforts are bent toward creating a world after their own imagination. Books like the Sixth and Seventh Book of Moses and *The Egyptian Secrets* are interesting to us only as a matter of curiosity. Yet, it is impossible to calculate the harm that may be done by allowing them to fall into the hands of people of this type.

Our most effective weapon in combatting the evils that may arise from the indiscriminate use, at the present time, of magical cures and ancient secrets is found in our educational system. Every effort should be made to advance the standards of our country school in order that their influence may be as effective and as far-reaching as possible.



## SMELL SHOCK.

RALPH R. FORAN, P. D.

Smell is the sense by which odors are perceived. We know that, in man, the organ of smell is the olfactory bulb, located at the anterior extremity of the olfactory tract of which it is an enlargement, the olfactory tract being a prolongation of the cerebrum. We further know that the development of this bulb bears direct relation to the acuteness of smell. But of the mechanism of olfaction we know very little. Various theories have been proposed to explain the why and wherefore of smelling, but all of them have largely failed to prove anything. It is one of the many unsolved riddles of life processes and we will have to take our first premise as a matter of faith.

The sense of smell is widely distributed throughout the animal kingdom. The lower animals, especially those breathing in water, become cognizant of the presence of odorous matter near them without touch, vision or hearing, and it is supposed that they do so by some sense of taste or smell, or a combination of both. Pharmacists may recall the sale of oil of rhodium, reputed by some fishermen to be an "added inducement" for fish which are otherwise shy of the bait. Most birds are probably without the power of smell, and in some, such as the frigate bird, the nostrils are obliterated. An instance is reported of three or four hens picking over a rubbish heap on which some calcium carbide had been thrown, and while the place reeked of acetylene the hens did not seem to mind it. Dogs, which are primarily dependent upon smell in their daily life, appear to be able to isolate a single smell component within a highly complex mixture. The fondness of cats for catnip, while unexplainable, is an indication of their acuteness of smell. In man the sense of smell is very feeble and imperfect in comparison with that of many animals, especially of the carnivores, which pursue their prey by scent, although it is declared that the half-savage Ainu of North Japan can track game like a dog, by the nose alone. James Mitchell, the English blind deaf-mute, recognized his friends when they came into a room, simply by their smell. Bucklan, the geologist, when riding once with some friends and the party lost their way and were overtaken by night, alighted from his horse, picked up a handful of earth, smelled it and at once declared they were near Uxbridge. He

knew the geology of the land and the smell of the soil. Generally speaking, however, the average man has limited olfactory power, unless he has improved the sense by exercising it.

In endeavoring to connect the sense of smell with the chemical constitution of the substance, Sir William Ramsay has pointed out that, as a general rule, substances having a low molecular weight have either no smell or simply cause irritation of the nostrils. He also shows that in the carbon compounds increase of specific gravity as a gas is associated to a certain point with a sensation of smell. It has also been pointed out that compounds of elements belonging to the same group, according to the periodic law, have sometimes odors of a similar character. But beyond this, there is no classification of odors. We must be content to describe an odor as pleasant, disagreeable, aromatic or characteristic and so on. This sort of description may mean anything or nothing, when it is considered that an odor may appeal to one person as being pleasant and to another as being obnoxious.

As to the intensity of odors, it is said that musk to the extent of only four one-hundredths of a milligram per liter of air is detectable and thus it is that a grain or two of musk will scent a room for years and at the end of the time no appreciable loss of weight can be detected.

As to the susceptibility of humans to odors, some persons may be sensitive to some odors while they do not recognize others. It is not uncommon for students to fail to recognize hydrocyanic acid in a solution given them for analysis.

The detection and identification of odors is of much importance to pharmacists and it was with the thought of determining their responsiveness that the following experiment was carried out. A series of fifteen liquid odorous substances was submitted to twenty men selected at random. Six of these men were members of the faculty of the Philadelphia College of Pharmacy, all of whom had had pharmaceutical training. Six were students with varying drug store experience and the remaining eight were graduate and practicing pharmacists. The purpose of the test was to identify specific odors and consequently color, taste and mobility were not to be taken into account. The substances submitted were as follows: Oil of turpentine, ethyl alcohol, oil of cinnamon, vinegar, oil of orange, kerosene, creosote, oil of sassafras, methyl salicylate, benzaldehyde, gasoline, ether, oil of anise, linseed oil and oil of nutmeg. The re-

sults of the experiment were both interesting and amusing. Oil of turpentine was recognized by all except three and these men called it in turn—oil of anise, oil of caraway and pine oil. Alcohol was difficultly recognized by the majority, a few claiming that it had no distinctive odor. One of the faculty of the College, after inhaling the liquid for several minutes refused to commit himself, although he said the odor was very familiar to him. Peculiarly, oil of cinnamon was reported as oil of anise, oil of bitter almond and oil of wintergreen by three of the contestants. Vinegar was easily recognized, although one of the men said that it reminded him of cheese. It was to be expected that oil of orange would be mistaken for oil of lemon and eight men reported the latter. The difference between the two is not very pronounced it is true, but to the trained nose is readily discernible. Kerosene and gasoline were confusing to quite a number, indicating that gasoline is not what it is "cracked up" to be. Why two men should report gasoline as chloroform is beyond explanation. Similarly, two men reported kerosene as carbon disulphide. Ten men judged wrongly on creosote. Five reported oil of clove, and the other five reported cresol. Those who were unsuccessful in identifying oil of sassafras and oil of anise, said that they recalled the odors as being those associated with salt water taffy. Only two men failed to identify methyl salicylate (synthetic oil of wintergreen), and singularly both of them reported oil of peppermint. Running true to form, benzaldehyde was twice mistaken for nitrobenzene (oil of nirbane). Only one man failed to recognize ether. He reported this as ethyl nitrite, at the same time reassuring himself by saying that he had worked with this substance at college while doing thesis work. Nine men were able to identify the odor of linseed oil. The others reported it variously as fish oil or cod liver oil and one said it was neatsfoot oil. The similarity of odor of linseed oil and cod liver or fish oil, is sometimes baffling unless the olfactory nerve is highly trained. The identification of oil of nutmeg was not attempted by three of the men, three reported oil of turpentine one reported it as oil of colander and one as oil of cardamom.

It is significant to note that the sense of smell in one of the students examined was almost nil. He admitted that he detected only the most powerful odors and that he never noticed the odor of hydrogen sulphide in the laboratory, although his desk was less than six feet away from the hood where this gas was generated and used

continuously. One of the men was suffering from a severe "cold in the head," and while generally an inflammation of the nasal passages deadens the sense of smell, this man made a score of eighteen out of the twenty. Also, another apologized that he "didn't smell very good."

We have something to learn from this simple test, and that "something" is that we have been neglecting the education of our nose. The identification of substances by the sense of smell is a thing which cannot be taught. It must be acquired by the process of exercising the function. Only "your nose knows."

TECHNICAL CHEMISTRY LABORATORY,  
Philadelphia College of Pharmacy and Science.  
June 10, 1921.

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## ABSTRACTED AND REPRINTED ARTICLES

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### A DREAM OF THE FUTURE.\*

By E. SAVILLE PECK, M. A., Ph. C.

PRESIDENTIAL ADDRESS DELIVERED BEFORE THE BRITISH  
PHARMACEUTICAL CONFERENCE.

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[The foregoing title may well be altered to American Pharmacy and its Possibilities and the dream which is so ably interpreted by Mr. Peck may also be the proper and happy aim of American pharmacy of the present day. Conditions related in this article are as vividly characteristic of our land as they apparently are of Great Britain and the remedies proposed for the correcting of these conditions should be quite as efficient for us and our calling as they are expected to be for our British conferes and their profession.  
—Ed.]

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On looking over the addresses of the distinguished pharmacists who have preceded me in this chair during the past few years, I find they can be roughly classified under four headings—those which deal purely with pharmaceutical science, those which have delved into the long-forgotten past, and endeavored from that rich field of

\*From *The Chemist and Druggist*, 1921, pp. 46-50.

experience to extract lessons for the present, those which have reviewed the pharmaceutical problems which presented themselves for solution at the time, and those which sought to peer into the future and visualize things that might be or ought to be.

The purely science side has been so ably presented by my immediate predecessor that I feel it is unnecessary on this occasion to develop that aspect of pharmacy. As to what has gone before, I was sorely tempted to write of the deeds of "our fathers of old," but finally decided that it might be more profitable perhaps if I endeavored to point out some of the anomalies which exist at the present time, and then to give free rein to my thoughts and aspirations by outlining some the "possibilities of the future."

#### CONFINING DISPENSING TO PHARMACISTS.

There are several precedents for so doing; there was the address by Dr. Tocher at Newcastle, in 1909, on "Should the Dispensing of Medical Prescriptions Be Exclusively Confined to Pharmacists?" in which, after recognizing that it had been a practice from time immemorial for doctors to supply physic direct to patients, he showed that the total transference of the dispensing of prescriptions from medical men to pharmacists would be accompanied by advantages to the medical man, the pharmacist, and the public. As a result of this address a Conference was arranged with the British Medical Association, and took place on May 19, 1910. There was a long discussion upon medical dispensing, prescribing by unqualified persons, and the sale of secret remedies, and it was also decided to set up a Joint Standing Committee, consisting of representatives of the two bodies.

The following year, however, Mr. Lloyd George introduced his National Insurance Bill. It is interesting to recall the fact that the Conference, through its executive, took immediate steps to put forward the claims of pharmacy, and this Joint Committee when it met passed the following resolution among others:

That the principle be affirmed that the dispensing under the Government scheme be done through the channels provided by the Pharmacy Acts, and that provision be made in the National Insurance Bill itself for the carrying out of the Chancellor's expressed intention that this work should be done by pharmacists.

The annual meeting of the Conference confirmed these resolutions of the Joint Committee, but the Council of the British Medical

Association added to the resolution the words "or by medical men." No other meeting of the Joint Committee was held, and the work of securing full recognition of pharmacy under the National Insurance Act was carried on by the Pharmaceutical Society.

I have recited all this to point out that the Conference did, in 1909, 1910, and 1911, take action in the matter of confining, dispensing to pharmacists, and to assert that, in my opinion, the time is ripe for another attempt to be made to carry the matter a step farther; and now that the dispensing for a large class of employed persons has been largely settled by National Health Insurance, to secure that this sound and salutary principle shall be applied all round. The Pharmaceutical Society has recently made a very important move in this direction by drawing the attention of the Government to the fact that in the recent Kidwelly case of poisoning by arsenic the medicine supplied to the patient was not dispensed by a pharmacist.

#### PRODUCTION OF THE PHARMACOPŒIA.

At the Jubilee meeting in 1913 you will remember that Mr. J. C. Umney, after reviewing the methods by which the various pharmacopœias of the world are compiled, advocated the appointment of a Commission, to be called the British Imperial Pharmacopœia Commission, which should consist of medical practitioners, registered pharmacists of Great Britain and Ireland, the Professor of Pharmaceutics of the School of Pharmacy, and others, and that this Commission should have the exclusive right of publishing, printing, and selling the Pharmacopœia. This plan follows the lines of the production and publication of the pharmacopœias of most other countries, and it is high time that steps should be taken to bring this dream of the future production of the British Pharmacopœia nearer to realization, or at least to see that pharmacists are represented on the Pharmacopœia Revision Committee. If this matter of the Pharmacopœia is considered impracticable, and nothing but a dream, there can be no doubt that there is a general desire on the part of medical men and pharmacists for the early production of another edition of our own British Pharmaceutical Codex. It is agreed on all sides that this is a most valuable work and has enabled pharmacists and medical men to co-operate very closely in the prescribing and dispensing of useful combinations of drugs to the mutual advantage of patients, medical men, and pharmacists.

PHARMACY IN THE ARMY.

In my address in 1915 I advocated the formation of an Army Pharmaceutical Service Corps, somewhat on the lines of that obtaining in many of the Continental armies. In this connection I may be permitted to state that the Army Council, in December, 1920, invited the Pharmaceutical Society to appoint three of its members to represent the Society upon a Joint Committee with the Royal Army Medical Corps, this Committee "to consider the employment of pharmacists in the Army in connection with the supply, distribution, and dispensing of medical and surgical supplies in peace and war, and to make recommendations regarding their organization and status." That Joint Committee, upon which I have the honor to serve, has met on several occasions, but has not yet presented its report, and its findings are still confidential. As one of the representatives, I should, however, like to say that I consider sufficient progress has been made to justify me in thinking that a marked and much-needed advance in the position of pharmacists in the Army will result as a consequence of the work of that Committee.

RESEARCH WORK.

Then, again, in 1919, Mr. Kirby in his address showed us the necessity for placing pharmaceutical research on a sound national footing, and, as you will see in the annual report, steps have been taken to place this matter before the Ministry of Health. These four addresses upon research, pharmacy in the Army, the British Pharmacopœia, and the question of dispensing may be considered by some to be but empty dreams and vague imaginings; but surely we may look upon them, if not as probabilities, yet at least as "possibilities of the future." Now, these addresses were given to gatherings of pharmacists and those interested in pharmacy, who were met together in conference primarily to advance pharmaceutical research and to inculcate and uphold a high standard of purity in medicines.

This Conference has no executive power such as that of the Pharmaceutical Society, and in this very fact lies at once its strength and its weakness. Its President for the time being is therefore entitled, and in fact it is expected of him, to throw out hints and make suggestions as to the aims and possibilities of pharmacy, and I intend

to take full advantage of this opportunity and venture to put forward ideas which doubtless some, to quote Tennyson, will consider

“Wide of the mark e’en for a madman’s dream.”

#### DEPRECIATING PHARMACY.

My dream, for such it may be considered, is of a time when pharmacy in this country shall, as has so long been the case on the Continent, have established itself as a separate professional entity—a distinct career—not merely as a handmaid to medicine, but as a calling collateral, co-existent and interdependent with medicine. Pharmacy as a distinct craft, calling, or profession has not yet materialized as have medicine, law, and accountancy. There is need for greater publicity as to the education and qualification required of the pharmacist and the functions pharmacy has carried on for many years with credit to itself and for the public safety.

This need of publicity is clearly seen in the much-discussed Dangerous Drugs Act Regulations. If the functions of the pharmacist had been more widely understood and appreciated, it is inconceivable that the Home Office should have suggested regulations for the sale and dispensing of scheduled poisons which are in themselves a redundancy and already very largely covered by the Pharmacy Acts.

Let us consider how pharmacy is visualized by “the man in the street.” In the main I suppose one must grant that he would look upon the pharmacist as the man who runs a chemist’s shop or dispenses medicine in a public institution, and would consider that those practicing this calling are not to be looked upon as men of education or of professional standing. There may be some ground for this point of view; but there are well-known exceptions, and many instances can be cited where individual pharmacists have achieved coveted positions in the scientific, archæological, political and municipal worlds. This has been due to the work that has been done by many outside their pharmacy and not because of their pharmaceutical qualification.

I recall an instance where a pharmacist read a paper of archæological interest at a meeting of a learned society after which a lady was heard to inquire: “Who is this Mr. X?” “Oh, don’t you know he’s Mr. X, the chemist.” “Dear me, I thought he was a gentleman.”

In the Army, notwithstanding the fact that the war was a great



"leveller," the same attitude was sometimes shown. I know of a case where an officer, who had all the qualifications necessary to fill a certain post but had in addition that of a pharmaceutical chemist was turned down, as he was informed, practically on this account. I do not consider this depreciation of pharmacy is due entirely to the fact that the practice of pharmacy is for the most part carried on "behind a counter" in "an open shop," but because the calling is so very "mixed"; it has many of the disadvantages of a profession and yet lacks the essential advantages of a trade.

#### IMPROVING THE STATUS OF PHARMACY.

I do not intend to be inveigled into an endeavor to differentiate between a trade and a profession, nor to affirm that one is more worthy, desirable, or honorable than the other. It can well be said that many so-called professional men carry on their profession in a purely commercial spirit, while many so-called tradesmen bring professional instincts to bear upon their business. Now, are we to be satisfied with the present condition of things and our existing standing in the public estimation? Do we wish to have the circumstances altered, and, if so, are we willing to purge ourselves of those things that militate against improvement, and also to put into operation certain influences that will make for greater efficiency and a higher position for pharmacy in the social scale?

Of course it is an essential consideration, which must precede any attempt to raise pharmacy to the status of a scientific and professional entity, that pharmacists must themselves wish for the elevation of their calling. Do they want to be recognized as possessing the technical knowledge and "competent skill" requisite for the practice of a profession, or would they rather simply draw their reward from protected profits on packed medicines? It is mere folly to complain, as some are apt to do, that pure pharmacy does not pay and leave it at that. It never will pay until it is acknowledged as an indispensable factor, with medicine in the nation's system of public health administration; and it never will be so acknowledged unless the will of the pharmacist is in and behind the movement.

One can do nothing for the men who want nothing and have no aspirations, but the possibilities are unlimited if the members of our calling really desire that pure pharmacy should be made to pay. I do not despise commercial acumen in pharmacists, and have

never condemned the "keeping open shop," but I do want to see it made possible for the pharmacist to make a living by pharmacy in that open shop, as well as elsewhere, and by virtue of his qualification, and not be forced to rely upon activities which do not call for a qualification at all. Shall we be content in the future merely to keep open shop and continue to carry on a purely commercial pharmacy, or shall we not combine in demanding an adequate remuneration for services dependent upon technical knowledge and competent skill and warranted by virtue of qualification? For those who have the necessary education, aptitude, and desire, should we not endeavor to carve out a more distinctly professional career? The scope of such a career could include the work of clinical pharmacists or clinical analysts, on the lines suggested for the Health Centres, of research workers in the large wholesale firms, and of teachers in the approved schools of pharmacy.

#### TWO CLASSES IN PHARMACY.

The question of the differentiation of pharmacy into two classes has for several years exercised my mind. I fully admit that, and that the subject bristles with difficulties and the magnitude of the task is obvious even upon superficial consideration.

To begin with, there is the difficulty of drawing a clear line between what is commercial pharmacy and what is clinical or professional. There is the training and examination essential for the one and unnecessary for the others. Then there arises the point as to where the differentiation as far as qualification is concerned should take place. In other words, where shall the differentiation between the business of a chemist and druggist and the profession of pharmacy come in?

On the Continent the division is made between those who can only sell drugs and certain poisons, and those who can be entrusted with the dispensing of medicines and physicians' prescriptions—with the addition in some cases of clinical analysis. In this country such an arrangement would not, I consider, at the present time be practical politics. The vested interests in dispensing are far too great, and, moreover the training required, and the standard of the examination demanded to qualify as a chemist and druggist, is probably sufficient for the duties he is called upon to perform at the present time. But there is the Major examination which could be extended

so as to include subjects which would cover clinical analyses, and the training for which would enable the student to undertake this work. The differentiation could take place here with less difficulty and disturbance than anywhere else—that is, because those who pass the Qualifying examination and those who elect to proceed to the Major examination and qualify as pharmaceutical chemists. I shall go more fully into this point later in my address.

#### CLINICAL ANALYSTS.

Here I would remind you of the report of the Consultative Council on Medical and Allied Services, which indicates that it is proposed that a Committee shall be appointed to investigate and report upon the question of what should be the future functions of pharmacists in relation to the services the Council were devising, and as to the most appropriate training and qualifications for those who are to perform these functions. In Section VI of this report it is stated: "It is a matter for consideration whether in certain cases, at any rate, individuals might not combine the duties of the pharmacist with those of the laboratory assistant."

This leads us to consider whether there is room for such trained men apart from the proposed Primary and Secondary Health Centres. Does the average general practitioner need the assistance of a trained clinical analyst to aid him in diagnosis and subsequent treatment? Would there be sufficient demand for such work in towns of, say, over 50,000 people to warrant the pharmacist in acquiring the requisite knowledge and setting up the necessary bacteriological and chemical laboratories for this purpose? I think there is room for such a development, especially where there is not at the present time a clinical institute providing for such work in the neighborhood. In connection with this there are several wholesale houses, especially those with a retail branch, who need men qualified to undertake this work.

I have recently visited the laboratory of a pharmacist where, in addition to a very flourishing business as a pharmaceutical chemist, he carries on an extensive bacteriological practice. He conducts urine analyses, both chemical and bacteriological, carries out blood-counts, the examination of secretions for tubercle bacillus, diphtheria, etc., the Wassermann reaction, and the preparation of autogenous and other vaccines. This pharmacist invites and encourages inspection

of his laboratory, and argues that it is better to demonstrate by actual work of this kind than to advocate it by discussions and papers upon the subject. Surely such work can be carried out at other centres by men adequately trained for the purpose.

A pharmacist who is actively engaged in clinical work, and thus closely co-operating with medical men, is obviously bound to attract much of the important work of the preparation and dispensing of drugs. This will tend to relieve the commercial firms of some of the occupations and duties which they frequently assert do not bring a commensurate profit. The exploiting of dispensing at unremunerative rates to act merely as a "bait" for other business is reprehensible and unprofessional. If pharmacy is really to rise, phoenix-like, from the ashes to which it has been reduced, I am convinced it can only be by the evolution of a higher grade of pharmacists who shall be trained to do this kind of work and entitled to practice as clinical analysts and so make pharmacy a more definite professional entity.

#### PHARMACY IN THE UNITED STATES.

During the war I enjoyed the advantage of spending a year in the United States of America, and visited many pharmacies in different States and cities. It is neither untrue nor unkind to say that in the drug stores there pharmacy is very much more "mixed" than in Great Britain, but occasionally one did meet with firms where little else than dispensing of prescriptions and sale of drugs took place. On the other hand, the schools and colleges of pharmacy are of a very high order, and invariably connected with one of the State universities. The pharmaceutical syllabus consists of a minimum course of instruction of 1200 hours, and in addition to the subjects required for our own examination includes physiology, toxicology, and the action of drugs upon healthy and diseased organs.

It is interesting to note that a Committee of the American Pharmaceutical Association has recently reported upon and outlined a scheme for the institution of two classes of pharmacies—(a) drug-stores and (b) pharmacies. This scheme is given in detail in the *Pharmaceutical Journal*, May 29, 1920, and well deserves careful consideration. I refer to this, not with a view of suggesting that we should copy their ideas, but to indicate the trend of thought that is taking place in the United States of America. In short, therefore,

practically the whole of the European countries have these higher qualifications of pharmacists, and now America also is seriously discussing this question. Are we to be left hopelessly behind? I am convinced that the time has arrived when we must endeavor to reawaken in the rank and file of pharmacists more of the professional spirit and an outlook beyond the many profit-making schemes that are suggested to us week by week by clever and imaginative advertisers. We must not be content, on the one hand, to benefit by the protection and privileges of a profession, and on the other hand, seriously to compromise the situation by an attitude of complacent commercialism.

#### THE POLICY FOR THE FUTURE.

In the past we have been far too prone to be the butt of others, and have been content merely to defend our position and our rights. Let us in the future endeavor to use the other means of defense—that is, to attack the positions against us. In the war the immediate objective on most occasions was a short line of trench, some 80 to 100 yards away; but there were always many others beyond, and the final objective was almost present in the minds of those responsible for the “higher strategy.” What shall be our “final objective”? Nothing less than the evolution of a real profession of pharmacy. If we do not advance from our present position and secure that these clinical duties shall be performed by pharmacists, there is a grave danger that, with the surplus of medical men and women that will very likely occur in the next few years, we shall find that our objectives have been occupied by others. Besides those holding the medical qualification, there is already an indication that there may be other competitors, for I have recently heard of one school which advertises not only a course for the teaching of dispensing, but, in addition, courses in bacteriological and clinical analyses, which are stated to be framed to fit its students for posts under the Ministry of Health.

In short, my dream is of the institution of a qualification based upon the present Major—and, seeing that the term “Minor” is now obsolete, there is no point in retaining the word “Major”—to be called the Fellowship examination, and that powers should be obtained to entitle the holder to call himself a clinical analyst or clinical pharmacist or registered clinical assistant of the Pharmaceutical Society.

I believe I am right in thinking that some years ago an effort was made by a few prominent pharmaceutical chemists to establish an institute of clinical analysts, but for various reasons the project fell through. Could not the Society by means of its Major or Fellowship examination, take the place of such an institute, and so render unnecessary the formation of a body outside the Society?

It is repeatedly argued, and with good grounds, that the present Major qualification has little or no pecuniary or other value beyond the confidence which increased knowledge invariably gives; but if the attainment of this examination carried with it the right of registration as a clinical analyst of the Pharmaceutical Society and a Fellowship of the Society, it would immensely increase the value of such a qualification and tend to raise pharmacy in the public estimation.

It is my opinion that a qualification of this kind would attract good men, would be acceptable to the Ministry of Health, would fulfill a need that must arise in the future, and would, by a process of evolution perhaps rather than of differentiation, create a profession of pharmacy which would be collateral, co-existent and interdependent with the medical profession.

#### EXAMINATIONS REVIEWED.

If it is agreed that we should make this endeavor let us consider the influences we must set on foot to carry out our desires. First there is the question of preliminary general education; but, as I went into this subject pretty fully on a previous occasion and "in another place," I do not intend to say much now. But I should like to repeat that in my opinion it should not be too high a standard to require that every student before registration should pass one of the School Certificate examinations. These examinations have been recognized by the Board of Education as equivalent to and interchangeable with the examination for Matriculation at the Universities and other entrance examinations to professional studies. Apropos of this a very interesting paper was read by Dr. Henry L. Taylor, of Albany, New York, U. S. A., at the Eleventh International Congress of Pharmacy, in September, 1913, at The Hague, entitled "Pharmaceutical Education in Different Countries."

The passing of the Registration examination should, without

doubt, be completed prior to apprenticeship, and it should be a question of honor among pharmacists not to accept an apprentice or pupil until that person has so registered. On my visits to several schools where students have already begun their curriculum of study for Part I of the Qualifying examination I have frequently discovered instances where this point has been overlooked.

Secondly, there is the question of the present Qualifying examination for registration as a chemist and druggist. The division of the Qualifying examination into two parts, and the enforcement of a curriculum of study at approved institutions, is a step the importance of which cannot be over-estimated. I feel sure it will lead before long to a more thorough and permanent education in the sciences which underlie pharmacy, and incidentally to an increased percentage of passes in the examination. I do not advocate, at the present time at least, any serious extension of the syllabus either for Part I or Part II, although some rearrangement of the subjects and readjustment of hours would, in my opinion, be advantageous. I consider there is much to be said in favor of adding to the Qualifying curriculum some outlines of commercial science. If the main work of the chemist and druggist is commercial let that commerce be carried on in a scientific manner, I consider that the syllabus for chemistry, botany, and physics should be one that could be covered by a general elementary course in these subjects as arranged at University colleges and technical schools for students reading for the London Inter-Science examination, First M. B., and others. Personally I should welcome the introduction of written papers, and would be prepared to accept the certificates of certain other examining bodies in lieu of our own Part I—New Syllabus.

The real difficulty is the inability of teachers to deal adequately with the subjects in the time allotted. I am repeatedly told that a whole academic year is required for Part I, especially if the student intends to go on to the Major, or a degree of B. Sc., or the Fellowship of the Institute of Chemistry. Under the present arrangement the teacher finds that "either he has to work to a pattern to make the work of the examiner easy or he is tethered lest he lead his pupil to browse beyond the common plot."

As to the schools for Part II, they will need constant watching and nurturing by the Society, which should look upon them as

branch schools and supply them with diagrams, lantern-slides, and specimens of drugs, so as to humanize and render more practical the courses of instruction in the technical subjects. The teachers of pharmacy in these schools are, for the most part, enthusiastic, capable, and efficient, and endeavor to instil into the students a high ideal of pharmacy as a calling. In many of the schools the students have all the advantages of the corporate life of the college, and the comradeship of students working for the qualifications of other professions. This is in itself a great gain, and one which, indirectly, will do much to increase the prestige of pharmacy in the public estimation. Endeavors should be made to maintain in the mind of the student such ideals that in post-graduate life he may be the better able to take a leading part in the public life of pharmacy and of the country generally. The words of Sir Clifford Allbutt in his Presidential address to the British Medical Association last July can equally be applied to pharmacy. "He (the medical student) may leave his hospital school full of ardor and in rapid growth, but in practice his ardor cools and he drops into routine; or, at any rate, such is his peril, and so less and less may the doctor feel himself a member of a great profession; he may drift out of public affairs, his outlook and sympathies may shrink, his work become a trade, and his medical neighbor his 'opponent.'" It should be the aim of the reorganized local associations to encourage and stimulate among their junior members a continuance of the scientific spirit which they have acquired, at least to some extent at their college or school.

Then, lastly, there is the improved and modified Major examination, which I trust the Council of the Society will proceed with at an early date.

May I offer one suggestion? With a view to creating the qualification of clinical pharmacist it might be advisable to include practical physiological chemistry, and bacteriology (including clinical microscopy) among the compulsory subjects. If certificates of training and examination in these subjects from lecturers and examiners at a medical school similar to those required for the diploma of Public Health were accepted in lieu of the Society's examination in these subjects it would not only make for economy, but the final qualification would carry more weight with the Ministry of Health and medical practitioners.



TO RECAPITULATE.

Pharmacy, if it is to progress, will have to move forward with the advance of general education and of applied science. If it is to take up its position with other professional bodies it must bring its final qualification up to University and Continental standards. If we cannot differentiate between the druggist and the dispensing pharmacist we can at least endeavor to evolve a higher type of pharmacist on the lines suggested.

You will doubtless say that to carry all these things into effect will require an earthquake or a volcano. You will remind me that volcanoes are now extinct in this country, or regulated by formula to erupt only with mild propriety. But, at any rate, they may be considered as some of the "possibilities of the future," and an attempt can be made to bring them nearer to the realm of today. The President of the Society has outlined in his recent memorandum a scheme for organizing its members and associates into properly constituted associations which shall function as local branches of the Society. Two important objects of these local branches are:

- (1) To watch the professional interests of pharmacists.
- (2) To promote papers upon scientific, technical, and educational subjects.

It is just here, in these local associations, that the professional spirit of pharmacy should be reawakened and discussions encouraged upon various topics initiated by the Society, and possibly assisted by official speakers. To mention a few of these subjects the following might be cited:

- (1) Elementary education required for registration.
- (2) Conditions of apprenticeship.
- (3) The curriculum of study for the Qualifying examination.
- (4) The future scope of the Major examination.
- (5) The question of granting a Fellowship of the Society to those who proceed to the Major examination.
- (6) The work of the Ministry of Health and the duties pharmacists should be called upon to render.
- (7) The separation of prescribing from dispensing.
- (8) The representation of pharmacists upon the Pharmacopœia Revision Committee.

(9) The disadvantage of encouraging the sale and prescribing of medicines of unknown composition.

(10) The stimulation of practical pharmacists to contribute original work in the compilation of the British Pharmaceutical Codex.

All these subjects are well within the scope of the professional side of pharmacy and discussions upon these matters within local association would doubtless prove of great value. These associations or local branches of the Society could appoint delegates to an annual conference or federation, which would then focus the considered opinion of their members upon professional matters.

Then, again, the various schools of pharmacy would greatly benefit by an interchange of ideas, experience, and methods between the heads of their different departments. An annual conference of such teachers could take place with the object of promoting and advancing the interests of pharmaceutical education.

This brings me to my last point. The British Pharmaceutical Conference has done and is doing a great work in stimulating research and maintaining a high standard of scientific pharmacy. It has for over fifty years annually brought together pharmacists and others interested in pharmacy from all parts of the United Kingdom and Ireland and oft-times has welcomed those from the overseas Dominions. It has published a "Year-Book of Pharmacy," of which it may well be proud. It has received year by year the hearty welcome and enjoyed the unstinted hospitality of the local Committee, and especially of the municipal authorities of the cities at which its annual meetings have been held. It has been a reunion of those who for the most part have been imbued with a true professional spirit. It has received delegates from local associations, and has frequently discussed educational problems. Cannot the Conference absorb within its constitution and administration the suggested Federation of Local Associations and the Association of Pharmaceutical Teachers? Has the Conference the necessary authority and funds?

During the war the paramount necessity for unity of control was seen to be vital if victory was ultimately to be achieved. In British pharmacy today there is need for a closer union of "purpose, counsel and activity" of all those who are working for a full realization of the profession of pharmacy.

One of my dreams is of a central unifying association which shall bring together and co-ordinate those forces of which I have been speaking. The union of these forces—education, qualification, research, and professional conduct—should result in the evolution of a real profession of pharmacy, which, co-existent and inter-dependent with medicine, should work for the advancement of the health of the great nation to which we belong. Some of you may say:

“I talk of dreams,  
Which are the children of an idle brain,  
Begot of nothing but vain fantasy.”

May I not claim, at least?

“I had a dream, which was not all a dream.”

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## THE THEORIES OF BLOOD COAGULATION.<sup>1</sup>

By JULES BORDET,

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First of all, I beg of you to excuse my imperfect knowledge of the English language and to accept my best thanks for the honor you have conferred upon me by inviting me to deliver the Herter lectures. I shall try today to give a brief *résumé* of the chief theories which have been held concerning the mechanism underlying the coagulation of the blood. This phenomenon deserves our interest not only because of its physiological importance but also as a striking example of the resources of experimental analysis. It can occur *in vitro*, and this is a very favorable condition for the success of investigation. Nevertheless, and although it has been the subject of innumerable researches, up to the present time, its mystery has not been completely disclosed. You will not expect me to attempt a detailed review of the whole subject. I shall give only such broad outlines as will serve to make clear the

<sup>1</sup>Lecture I of the Herter Series, delivered before the Johns Hopkins University on Tuesday, October 26, 1920.—From the *Bulletin of the Johns Hopkins Hospital*.

modern conceptions which seem to afford the best explanation of this complicated process, and which, therefore, especially deserve our attention.

It is hardly necessary to remind you that coagulation is nothing else than the aggregation, into meshes of fibrin, of particles of fibrinogen, a substance which, as Fredericq showed 43 years ago, pre-exists as a dispersed colloid in the circulating plasma. When the blood flows from a wound, the first determining factor which, through successive modifications of the plasma, assures the solidification of fibrinogen, is not infrequently the mixture of the blood with very active principles liberated by the bruised tissues, or in other words, the addition to the blood of tissue extract. But such an influence is an additional one, foreign to the blood itself; hence, limiting the problem, I shall consider here, exclusively, the coagulation that the blood is capable of showing, solely by means of its own substances.

A most important, even a decisive factor of this automatic coagulation, is the contact of a foreign solid body (glass, for instance), which acts only physically by its presence, since it does not liberate any soluble substance. The contact, external factor, brings into activity the internal factor, belonging to the blood, and that is the process through which the principle directly and immediately responsible for the coagulation, the fibrin-ferment or thrombin, is produced. In fact, the thrombin, which is found in large quantities in the clot or in the serum, does not exist (as Schmidt showed many years ago), in the circulating blood. Consequently, several stages are to be distinguished in the total process, the most important one being the period in which the thrombin appears, the fibrinogen itself playing merely a passive rôle. Fibrinogen can be extracted by special methods and obtained in a fairly pure condition, but it must be kept in mind that the essential problem presented to the physiologist is the coagulation, not of pure fibrinogen, but of the blood considered as a whole, that is, of a very complex medium, cellular and plasmatic, having a definite reaction and definite osmotic pressure, containing numerous constituents, and especially colloids, which presumably are apt to influence each other through molecular adhesion. Coagulation could not be studied without taking into consideration every influence apt to interfere in the phenomenon.

Since the blood of mammals, as a rule, clots promptly, it seemed

essential to the success of the investigation to determine how the course of the process could be protracted and, moreover, how it could be stopped at the first period of its evolution, so as to make possible the separation of the cells from the still liquid plasma. Several methods have been devised; I shall mention them very briefly.

Concentrated salts, magnesium sulphate for instance, hinder the coagulation. Common salt especially answers the purpose, being a normal constituent of the organism.. Blood from the artery to which from three to five per cent. of salt has immediately been added yields by centrifugalization a clear plasma which does not clot so long as the high saline concentration is maintained, but which, when diluted with an amount of distilled water sufficient to re-establish the normal saline content, clots rather quickly. Decalcifying salts, the type of which is sodium oxalate, prevent completely the coagulation, calcium salts being necessary to this phenomenon. By centrifugalization a clear plasma is obtained, which tends to clot when a soluble calcium salt, such as calcium chloride, is restored.

Coagulation is also prevented if to the active contact of glass a contact is substituted, which is not, if we may so express it, felt by the blood or the plasma. A liquid does not feel a wall, I mean does not react physically to it, unless it is capable of adhering to it. Freund was the first to show that blood flowing from the artery does not clot, or at least clots very slowly, when received in a vessel the inside of which has been coated with oil or vaseline. Since it forms a solid coating, paraffin is very suitable to such experiments, and frequently permits the separation of the cells and the plasma by centrifugalization. In conjunction with Gengou I observed that by these means a clear plasma can be obtained and be kept fluid for twenty-four hours, but that clotting soon occurs when the plasma is brought into contact with glass. This experiment shows that the contact of glass can bring about its effect without the presence of any cells, that is, without any vital interference—we have to do with a physico-chemical phenomenon.

The blood of certain animals, namely, birds and fishes, as Delezenne has shown, clots very slowly by itself, coagulation being greatly hastened by the addition even of traces of tissue extract. Without the help of decalcification or of paraffin coating the blood of a bird will remain fluid for a long time and even yield by centrifugalization a permanently liquid plasma, provided that the tube in-

serted into the vessel has not been allowed to touch the wound, and consequently no trace of tissue extract has become mixed with the blood. As a matter of fact, this precaution ought to be taken regularly, whatever may be the species of animal under experiment, as it is quite a general rule that tissue extract accelerates coagulation, this auxiliary influence being particularly noted for birds, because this blood is not so capable of spontaneous coagulation as is that of mammals.

Thanks to such methods, the separation of the two constituents, cells and plasma, can be attained before any beginning of coagulation and—let us emphatically insist upon this essential fact—before any appearance of the coagulating principle, thrombin. There is no need to remind you that serum yielded by coagulation contains thrombin.

We must now try to go further and subject plasma and cells to a closer analysis. Let us consider first the plasma. Soluble calcium salts are necessary to coagulation. How do they act? Pekelharing and Hammarsten have shown the essential fact that these salts are not necessary to the transformation of fibrinogen into fibrin under the influence of thrombin, but are indispensable to the formation of the latter, that is, to the production of thrombin from the mother-substances already present in the circulating blood. The production of thrombin is prevented by oxalate, but on the other hand decalcification does not prevent the coagulation of the fibrinogen by completed thrombin. Indeed, it has been proved that blood, oxalated immediately after withdrawal from the artery, remains permanently fluid, no thrombin being ever detected in it, whereas if serum yielded by normally clotted blood be oxalated, this oxalated serum, added to oxalated plasma, causes the coagulation of the latter. From these facts it follows that oxalated plasma is a most suitable reagent for the detection of thrombin in a given liquid; indeed, an estimation of the coagulating power of such a liquid may be made by taking into consideration the quantity of oxalated plasma coagulated by a certain amount of this liquid, or the rapidity of the occurring coagulation. But it must be borne in mind that, at least when present in serum, the activity of a given thrombin depends not only upon its quantity but also upon its age. The capacity of fresh serum to coagulate oxalated plasma decreases very quickly, by a spontaneous attenuation of the thrombin, and this

fact affords a possibility of detecting whether a given thrombin has been produced quite recently or some time ago. Several experiments, as we shall see, require such a determination.

Contact is also necessary to coagulation. How does it operate? I showed with Gengou, many years ago, that contact is in a way analogous to calcium, or in other words, that contact with a foreign solid body (paraffin of course excepted) is necessary to the appearance of thrombin, but is not requisite for the coagulating influence of the latter. When blood is received into a paraffined vessel, thrombin is not formed; when received into a glass vessel, thrombin is produced in the zone of contact, a fact which explains why coagulation begins along the wall. But when serum yielded by previously clotted plasma is added to blood or plasma kept in a paraffined vessel, the entire mass rapidly solidifies the paraffin no longer exerting any inhibiting influence. This experiment explains why blood freshly drawn and placed in a glass vessel coagulates in a mass much more rapidly when shaken.

What then is the origin of thrombin? It does not exist as such in the circulating blood, although the latter contains everything requisite for its production. The circulating blood, therefore, contains the mother-substance, or mother-substances, of thrombin, which, for convenience, may be called prothrombin, and which in the early stages of coagulation is converted into thrombin. What is prothrombin?

Sixteen years ago Morawitz made an important discovery in this connection. He found that if crushed tissue, muscle for example, is added to serum yielded by normal coagulation, the coagulating power of this serum towards oxalated plasma is considerably increased. And yet, the extract of tissue by itself does not contain any thrombin, since without the help of serum, it is incapable of coagulating oxalated plasma. Hence, we are forced to conclude that the tissue extract contains something which is not thrombin, but which reacts with the serum so as to produce this active principle. Thence follows at once the hypothesis that thrombin is derived from the interaction of two different substances, the one furnished by the tissue cells, the other by the serum. Undoubtedly, even before the introduction of the tissue extract, a certain amount of thrombin existed in the serum, but it seems as if this fluid contained also an excess of the mother-substance, the latter being capable of reacting

with the tissue extract so as to generate a fresh supply of thrombin.

But the question immediately arises whether such an assumption, deduced from experiments in which tissue extract plays an important rôle, may be without further question applied to the automatic coagulation of pure blood. As a matter of fact, it must be kept in mind that injected into the circulation, the tissue extracts are highly toxic, causing sudden death due to intravascular coagulation. Undoubtedly they contain some coagulating principle foreign to the blood itself. This substance upon which I shall not dwell today, our present task being merely the study of the coagulation of pure blood, in all probability, is of an albuminoid nature, and is markedly thermolabile. It is specifically related to the tissues, does not exist in the blood, and could not be considered as a real mother-substance of thrombin. But we must immediately add that, besides this peculiar principle, the tissue cells, nevertheless, contain one of the two mother-substances of thrombin. This exists also in the blood cells, is of lipoid nature and may be designated *cytozyme*. The other mother-substance, called by us *serozyme*, is furnished by the blood fluid and is present in the serum. But let us see how these determinations have been arrived at?

The assumption that the blood cells furnish one of the mother-substances of thrombin is in perfect accordance with the results of experiments dealing with the part played by those cells, and chiefly by platelets, in the coagulation. Platelets can be easily separated by centrifugalizing oxalated blood at a moderate speed for a short while; being very light, they remain in suspension, whereas red and white corpuscles are thrown down, the turbid supernatant fluid pipetted off being very rich in platelets. Now if such a platelet-plasma is centrifugalized for a long time and at a very high speed, the platelets finally are sedimented and a clear plasma may be obtained from which the platelets have not been thoroughly eliminated, this being impossible, but in which they are present only in small numbers. Comparing these two plasmas, the one very rich, the other very poor in platelets, Lesourd and Pagniez found that after recalcification the former clots rapidly, the latter slowly. Completing these experiments, with Delange, by comparing the coagulating influence, on oxalated plasma, of the two serums yielded respectively by the coagulation of plasma rich in platelets and of plasma poor in plate-



lets, we observed that the former serum contains a much larger quantity of thrombin than the latter. Consequently, the platelets actively participate in the production of the coagulating principle. This fact can be proved more distinctly by the following experiment: A sediment constituted exclusively of these small cells is obtained by vigorously centrifugalizing oxalated plasma, previously freed of its red and white corpuscles, but containing still its platelets. This platelet deposit, thoroughly washed, is emulsified in physiological solution, and one drop of the turbid emulsion thus obtained is added to a certain quantity of a serum which, being derived from the slow coagulation of recalcified oxalated plasma that has been freed of its own platelets, is by itself very poor in thrombin. Within 20 or 30 seconds, the mixture becomes capable of coagulating a suitable amount of oxalated plasma almost instantaneously; in other words the reaction of serum with platelets generates an abundant supply of thrombin. It must be pointed out that this experiment closely resembles that of Morawitz except that platelets instead of tissue cells are added to the serum. Tissue cells and platelets both contain one of the generators of thrombin, which may be called *cytozyme*. The second one, the *serozyme*, exists in the serum. It can be easily demonstrated that the reaction between serum and platelets, that is to say, between serozyme and cytozyme, takes place only in the presence of soluble calcium salts, no thrombin appearing if the serum has been decalcified before the introduction of the platelets. Moreover, I shall further insist on the fact that the two substances unite, that they really consummate each other. Indeed, experience shows that when a serum has been treated once with platelets, and has yielded thrombin, this serum is subsequently incapable of reacting with a new amount of platelets, its serozyme having been exhausted by the first reaction. It follows that a serum produced by the coagulation of a plasma rich in platelets and which of course contains much thrombin, is considerably less rich in serozyme, that is, considerably less capable of reacting with new platelets, than is a serum derived from a plasma deprived of most of its platelets. This is precisely what experience shows. It is, therefore, highly advisable always to employ for serozyme a serum obtained by the coagulation of oxalated plasma which has been carefully freed of its platelets before recalcification.

Serozyme is a thermolabile substance, easily destroyed by heat.

No thrombin is produced when platelets are added to serum that has been exposed to a temperature of about 56° C. On the contrary, cytozyme, the active principle of platelets, may be heated to a hundred degrees and even higher without losing its properties; cytozyme is thermostable and, furthermore, can be easily extracted.

A thick emulsion of platelets, treated with a large excess of absolute alcohol, gives an extract from which, by evaporation a residue is obtained which is soluble in alcohol, ether, toluol and chloroform but insoluble in acetone, thus exhibiting the characteristics of lipoids, and especially of lecithin. This residue acts as a very powerful cytozyme.

As we were able to show eight years ago traces of this lipid behave exactly as do platelets, generating thrombin when added to serum, hastening the coagulation of recalcified oxalated plasma or causing the coagulation of spontaneously non-coagulable bird's plasma. The same lipid, possessing exactly the same properties may be extracted from tissues, from muscle for example. Cytozyme is thus a lipid.

These facts having been obtained about cytozyme, what is serozyme? Serozyme is certainly furnished by the plasma, not by the cells. Platelets contain cytozyme; they yield thrombin when mixed with serum but they are never able to liberate thrombin when kept in physiological solution or in distilled water, even in the presence of calcium salts. They consequently contain only one of the mother-substances, not both of them. The liability of serozyme towards heat allows us to presume that this substance is of an albuminous nature. Its fragility would be a very serious hindrance to its isolation, but for one of its properties—a really fortunate one. The serozyme shows a strong tendency to adhere to mineral precipitates, barium sulphate or calcium fluoride for example. This is the reason why, as I discovered many years ago with Gengou, those precipitates, added to oxalated plasma wholly suppress in the latter the property of coagulating by subsequent recalcification; one of the mother-substances, the serozyme, which is absolutely requisite for the production of thrombin and consequently for coagulation, has been entirely removed. I have found more recently, in conjunction with Delange, that tricalcic phosphate is especially powerful as an absorbent. When diluted in physiological solution, this substance gives a rather gelatinous emulsion, a very slight quantity of which,

added to blood flowing from the artery, prevents its coagulation. By centrifugalization and pipetting off, a clear plasma is obtained, which remains fluid, even when platelet emulsion, or tissue extract, or lipoidic cytozyme, is added. This is easily understood; both mother-substances, serozyme and cytozyme, are equally necessary to the production of thrombin; it is of no use to add one of them if the other is absent. But such a plasma, which we may for the sake of brevity call "phosphate plasma," clots under the influence of thrombin or, which naturally is the same, when both mother-substances are added. It behaves as an excellent reagent for the detection of thrombin. Since its composition closely resembles that of the original plasma, it may be considered as being fibrinogen dissolved in a normal medium.

But tricalcic phosphate is endowed with a property which is remarkably useful for technical purposes. As is well known, it is capable of being dissolved in physiological solution under the influence of a current of carbonic oxide gas. Consequently, phosphate which has been added to plasma and has absorbed the serozyme, after having been thoroughly washed, can liberate, thanks to its own dissolution, the active principle it had withdrawn. In this way, Delange and myself succeeded in bringing about the isolation of serozyme, which, on the addition of cytozyme extracted from platelets, gave abundant thrombin. Thus in the course of the whole experiment the factors which determine coagulation are in reality subjected to an analysis followed by a synthesis.

As mentioned above, our assumption that serozyme and cytozyme are the generators of thrombin involves the idea that those mother-substances really unite to form a compound, which is thrombin. This ought to be demonstrated also with regard to pure cytozyme. I mean a cytozyme in the condition of a lipoidic extracted matter. If the union really occurs, we may anticipate that, if a given quantity of serozyme be mixed with a sufficient amount of cytozyme, thrombin will be engendered and the serozyme will be exhausted; in other words, it will be no longer capable of yielding fresh thrombin when a new amount of cytozyme is added. Such is indeed the case. Serum yielded by coagulation of recalcified platelet-free oxalated plasma is divided into two parts, lipoidic cytozyme being added to one of them, the other portion being kept as it is. In the tube containing both serum and cytozyme, thrombin

appears, the activity of which is very strong at the outset, but decreases as we know, very rapidly, so as to become quite attenuated by the following day. On the next day, lipoidic cytozyme, and, several minutes afterwards, oxalated plasma are added to both tubes. Then the tube which has received cytozyme on the preceding day does not clot at all, or does so only very slowly, whereas the tube, to which cytozyme has just been added for the first time, clots almost instantaneously.

It is clear that such an experiment makes it possible to ascertain whether the same cytozyme, endowed with the same binding properties as the pure lipoid, exists in fresh or heated platelets, or in tissue juice, ground muscle for example. Adequate experiments show that serum which has already reacted with any one of such materials does not generate any more thrombin when subsequently brought into contact with any one of them. For example, serum to which lipoidic cytozyme has been added will not react any more either with the same lipoid, with platelets, or with muscle juice, and conversely.

Without entering into details, I may add that the manner in which the two substances unite closely resembles the mode of union of toxins and antitoxins, in that the process is not governed by the law of strict and constant equivalents, but takes place in varying proportions, thus seeming to result not from true chemical affinities but from contact affinity or molecular adhesion. But another fact, more noteworthy for its bearing upon the underlying mechanism of coagulation is disclosed by the determination of the lapse of time required for the union of both substances.

Serozyme being found in serum may be assumed to exist also in the oxalated plasma from which this serum has been derived. Now if cytozyme and serum are mixed, thrombin appears very quickly; it is only a question of some seconds. But—and this fact is undoubtedly remarkable—if cytozyme be added, not to serum yielded by coagulation of recalcified oxalated plasma, but to an identical oxalated plasma recalcified just before, that is, at a moment when this plasma is still perfectly fluid, the appearance of thrombin is greatly delayed. In other words, serozyme reacts with cytozyme quickly when present in serum, slowly when present in plasma. We thus reach the conclusion that the serozyme does not exist in the same condition in plasma as in serum, that in plasma it is not

capable of reacting at once with cytozyme. We may express this fact by saying that plasma contains proserozyme instead of active serozyme, one of the first phenomena of the whole process of coagulation being precisely the conversion of proserozyme, unfit until transformed to unite with cytozyme, into serozyme capable of this reaction.

The notion that in original plasma or in circulating blood, serozyme does not exist as such, that is, does not exhibit affinities toward cytozyme, satisfactorily explains why intravascular injections of the latter substance are, as we found, quite harmless. But the blood of such injected animals shows, when shed within about half an hour after the injection, a strikingly increased tendency to rapid coagulation. This fact as we have pointed out may probably be available for therapeutic purposes in cases of hemorrhage.

Is it now possible to investigate under what influences the proserozyme is converted into serozyme, in other words, under what influences does it acquire the capacity of reacting with cytozyme?

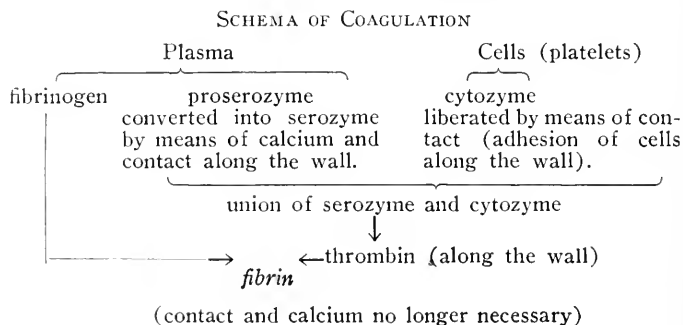
To solve this problem, we have at our disposal a very adequate technic, based on the use of oxalated salt-saturated plasma.

Some minutes ago I mentioned the fact that when oxalated plasma is saturated with common salt, the fibrinogen is entirely precipitated. After strong centrifugalization, pipetting off and elimination of the excess of salt by dialysis in presence of physiological oxalated solution, the supernatant fluid represents exactly normal oxalated plasma, except that, having lost all of its fibrinogen, it cannot coagulate. Being oxalated it does not contain any trace of thrombin, but is still capable of producing plenty of it on the addition of calcium salt and cytozyme. Now if a calcium salt and cytozyme are added thrombin appears indeed, but only after a rather important delay. Half an hour, and sometimes more, must elapse before the mixture becomes capable of bringing about an almost instantaneous coagulation of a fibrinogen solution. Thus the acquisition of the ability to react with cytozyme, that is, the conversion of proserozyme into serozyme, requires a notable length of time. Now, on the other hand, if the aforesaid fluid without fibrinogen is recalcified and cytozyme is added one or two hours later the thrombin appears almost instantaneously. This experiment clearly illustrates the essential assumption that the whole process of the production of thrombin, the first stage included, which is the conversion of pro-

serozyyme into serozyyme henceforth capable of uniting with cytozyme, takes its course without any participation of fibrinogen.

Furthermore, the conversion of proserozyyme, which as we know cannot take place without calcium salts, is—and the fact is noteworthy—strikingly favored by contact with glass. The capacity of reacting with cytozyme appears only after a much longer lapse of time when the recalcified fluid is kept in a vessel coated with paraffin. Consequently, the influence of contact, which is so obvious in coagulation, is not exerted through some interference of fibrinogen, but really acts without any help of the latter, as a factor of thrombin production. It is highly probable that contact by way of absorption, frees the liquid of some antagonistic substance, most likely some protective colloid, which prevented the serozyyme from reacting with cytozyme, that is, maintained it in the inactive condition of proserozyyme. On the other hand, experiments show that the presence of cytozyme likewise facilitates such a liberation of serozyyme, owing to its strong affinities towards the latter principle.

To sum up, we are now able to follow the schema which indicates the order of succession of the phenomena.



I think that the schema symbolizes quite accurately the most prominent features of the whole process and distinctly shows the sequence of events. But the mechanism underlying coagulation as it occurs under ordinary conditions is still somewhat more complicated, owing to a peculiar property of thrombin. Thrombin results from the union of serozyyme and cytozyme, but these two substances combine in variable proportions. The consequence is that a given complex, when rich in serozyyme, is able to capture an additional amount of cytozyme, and, when rich in cytozyme, which

is ordinarily the case in the coagulation of whole blood, shows a marked affinity towards a new amount of serozyme. As a matter of fact, such an affinity is so strong that it causes thrombin to attract and to possess itself of serozyme even when this principle is still present in a state of proserozyme. Consequently, finished thrombin acts as though it could bring about a remarkably quick conversion of proserozyme into serozyme, the process preliminary to the genesis of fresh thrombin being thus greatly hastened. The consequence is that, when thrombin is added to oxalated plasma which has been just recalcified, the total amount of thrombin this quantity of plasma is apt to furnish appears much more rapidly than it does when the same plasma is allowed to clot spontaneously without the stimulus of thrombin. In fact, thrombin itself thus accelerates the formation of thrombin. Owing to lack of time, I cannot report here in detail the experiments which have established this idea, but shall now consider briefly some of the views held by certain authors and which are not in agreement with the ideas developed above.

As is well known, my countryman, the physiologist Nolf, has adopted the rather startling theory of Wooldridge according to which, instead of being the immediate determining factor of coagulation, thrombin is generated as a consequence of the coagulation itself. According to Nolf, the transformation of fibrinogen into fibrin is not the effect, but the necessary condition of the appearance of thrombin. Many of the data which I have recorded above energetically plead against such a conception. For example, I would only recall the experiments showing the production of thrombin in fluids altogether devoid of fibrinogen, and thus proving unquestionably that fibrinogen does not play any rôle in the production of the coagulating principle.

One important point has been and still is controverted. I mean the true significance of the lipoid to which we have so often alluded. Schmidt, who had already observed the accelerating influence on coagulation, exerted by alcoholic extracts of tissues, believed that such lipoids rendered easier the production of thrombin, without assuming, as I do, that they really enter into its constitution. One of the most distinguished among the writers who have devoted their skill to the study of coagulation, Professor Howell, especially directed his attention towards the fact that the lipoid extracted, for example, from nervous tissue, is capable of

inducing the coagulation of peptone plasma and hirudin plasma which, as is well known, remain fluid because they contain an anti-coagulating substance, called antithrombin. In opposition to our assumption, Howell thinks that the lipoid is not a constituent of thrombin, but acts by neutralizing the antithrombin, which hindered the spontaneous conversion of prothrombin into thrombin. The real existence of antithrombin is of course unquestionable and it has been proved beyond doubt that antithrombin may be neutralized by thrombin, the two substances being, in all probability, capable of forming a compound. Now the question arises whether, when lipoid is added to peptone or hirudin plasma, the removal of the antithrombin function is due, as Howell claims, to the direct neutralization of antithrombin by this lipoid, or to a neutralization of antithrombin by thrombin generated under the influence of the same lipoid, the latter reacting with the serozyme or proserozyme also contained in the aforesaid plasma. In other words, according to this second interpretation, the neutralization of antithrombin by the lipoid would be merely apparent or at least indirect, the direct agent of this neutralization being the thrombin which the lipoid has caused to appear. I believe that such a conclusion is forced upon us by some recent and careful experiments by Gratia. Without entering into the somewhat complicated details, they have shown that the lipoid does not at all neutralize the antithrombin when the serozyme or proserozyme has been previously removed, that is, when the production of thrombin has been made impossible. Even when the lipoid is added in large excess, the abolition of the antithrombin function occurs only in proportion to the amount of serozyme present, that is, in proportion merely to the quantity of thrombin that can be generated. Consequently, a direct influence of the lipoid on the antithrombin cannot be admitted.

Furthermore, Howell's view could hardly be brought into harmony with a very essential fact, which has been mentioned above. Were his assumption correct, it should be admitted that serum yielded by the coagulation of recalcified oxalated plasma deprived of its platelets contains a large amount of antithrombin, since the addition of lipoid to such a serum, itself poor in thrombin, produces in this fluid plenty of the latter principle; upon the whole, the serum should in this respect resemble very closely the plasma from which it is derived. But, such being the case, it would be very difficult to



understand why the lipoid neutralizes the antithrombin very quickly when added to serum, and very slowly when added to plasma. I think the only possible explanation of such a difference is that in serum but not in plasma, as was said before, the serozyme is capable of reacting very rapidly with cytozyme to generate thrombin. However, the question as to the relation of cytozyme to the antagonistic function is one of the most delicate in the whole study of coagulation and I fully realize that different views may still be upheld. As I told you at the beginning, coagulation has been studied for years and years by many investigators; none of them can presume that the problem is yet solved; every one of them merely indulges in the hope of gathering some complementary data; a little more information.

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## ATROPINE SULPHATE FROM DATURA STRAMONIUM.\*

By H. W. RHODEHAMEL  
and E. H. STUART.

An interesting and valuable lot of data concerning the preparation of atropine from *Datura Stramonium*, commonly known as Jimson weed, is presented by the authors.

The percentage of total alkaloids in the plant is said to vary from 0.15 to 0.6 per cent. The seeds contain the highest amount, next come the leaves, and the lowest amounts are found in the stems, particularly in the woody portions, where the figure runs below 0.10 per cent.

The method of extraction was by the use of 0.2 per cent. aqueous solution of sulphuric acid preserved with 0.5 per cent. of formaldehyde.

The dilute solution of atropine sulphate was treated with Lloyd's reagent, which consists of a hydrated siliceous (Fuller's) earth.

Different fractions of the percolate were treated with appropriate amounts of Lloyd's reagent, after which the reagent was allowed to settle, the exhausted percolate was decanted and the precipitate drained and thoroughly dried at a temperature of about 50° C.

The percentage of alkaloidal material recovered from different

\*Abstract of a publication from the Research Department of Eli Lilly & Co., Indianapolis, Ind.

lots ranged from 33.98% to 93.06%, the larger amounts being recovered when larger proportions (359 pounds to 5000 gallons, representing 15,500 pounds green *Stramonium*) of the reagent was added.

The adsorbed alkaloids were recovered by extraction with ether after making alkaline.

The reagent, after extraction, always contained about 0.2 per cent. of alkaloid, which could not be economically removed.

Experiments in which other acids were used to facilitate extraction showed no marked differences from those recorded, although other preservatives, such as bleaching powder, cresol, and sodium bisulphite, gave better results than formaldehyde in the matter of the yield of alkaloid.

The crude alkaloidal material recovered from the "reagent" was purified as follows:

#### PURIFICATION OF THE CRUDE ATROPINE.

The alkaloidal material was extracted from the Lloyd's reagent with 95 per cent. alcohol, using lime to obtain the proper alkalinity. The extractions were acidulated with acetic acid and the solution concentrated first to 12 per cent., and then under diminished pressure to 2 per cent. of its original volume. This procedure was sufficient to convert all the hyoscyamine into atropine. After neutralization with ammonia, the solution was allowed to stand over night and filtered. A test portion of the filtrate was shaken with ether. If an emulsion resulted, the solution was diluted about one-fourth and returned to the vacuum still. Distilling the neutral liquid, and again filtering, usually prevented the troublesome emulsion with ether. Ammonia was added until the solution was alkaline and the atropine alkaloid extracted with ether. After evaporation of the ether, the alkaloid was carefully dried at about 35° C.

The dried alkaloid was dissolved in ethyl alcohol in the proportion of one ounce of alkaloid to two fluid ounces of solvent, and the solution almost neutralized with sulphuric acid, using cochineal as indicator. After filtering it was evaporated on the water bath to a thin sirup, and to this sirup, while still warm, acetone was added almost to the point of precipitation of the atropine sulphate.

On cooling, the atropine sulphate crystallized. If not sufficiently

pure the crystals were dissolved in alcohol and recrystallized as outlined above.

The acetone was evaporated from the mother liquor, and the alcoholic solution of atropine sulphate poured into a large volume of water. From this the alkaloid was extracted with ether, and if not of sufficient purity the process already outlined was repeated.

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### DRUG RESEARCH.\*

Declaring that all humanity would be benefited by the establishment of a \$10,000,000 national institute of drug research in the country, Edwin E. Slosson, editor of the *Science Service* of the National Research Council, in a recent address before the American Drug Manufacturers' Association in Washington, D. C., stated that the making of drugs was developing along the lines of discovery and cultivation of new medicinal plants and in the invention of synthetic remedies. He said in part:

"The day of the shotgun dose has gone by. The modern doctor uses a rifle. In former times it often happened that the antiseptic aimed at a bacillus and killed a phagocyte. Before the era of recent research the best of antiseptics was carbolic acid. Yet carbolic acid applied to a wound killed off the invaders and defenders of the bodily citadel with almost equal impartiality. This is as if the United States entering a war in defence of France, had showered poison gas all along the front and wiped out both the German and French armies.

"The Bible recommends us to beat our swords into plowshares, but the chemist has gone farther in turning a poison gas into a perfume. The war delivered into our hands a chemical industry for which we were not fully prepared and by which we have not fully profited. We are now producing more tons of dyestuffs than we formerly imported, but some of the most important dyes are not yet made in America. In the field of pharmaceutical research I am told that we are not even keeping up with the procession, to say nothing of leading it. The plan proposed by the American Chemical Society for a national institute of drug research with an endowment of \$10,000,000 ought to be carried out, for it would benefit not only our own country but all humanity.

\*Through the *Canadian Pharm. Journ.*

"In the drug business there is opportunity for development in all three of these lines. First, in the discovery of new medicinal plants; second, in their cultivation for the increase of the active principle; and third, for the invention of synthetic remedies. A pharmaceutical survey should be made of the tropical territory under the control of the United States and whenever any plant is found which may reasonably be suspected of concealing anything of value about its person it should be taken into custody and placed in a reformatory where its principle might be strengthened.

"The misnamed vitamins are now being separated and concentrated and may eventually be produced as pure chemical compounds which may be administered in a pill to correct a deficiency of diet. Possibly they may be made synthetically and even now vitamins are invented that will stimulate the growth of a particular organ or regulate some specific bodily process. But we shall not have to resort to vitamin pills if we plan our diet properly.

"Here is the borderland where foods and drugs come together, and I venture to predict that the distinction between them will ultimately be wiped out. I believe that the doctors will become dietitians and drug-manufacturers will devote themselves largely to the preparation of regulated foods. Bran biscuits may well serve as substitutes for Epsom salts and air-dried spinach for iron citrate. In other words, I look for the merging of medicine into hygiene. There will be less need for remedies when more attention is paid to preventives."

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#### ,OIL OF CADE.\*

By C. T. BENNETT, B. Sc., F. I. C., F. C. S.

Pharmaceutical Chemist.

"Huile de Cade" has always been somewhat variable in character, particularly as regards specific gravity. According to the British Pharmacopœia, the specific gravity is "about 0.990," but during the last few years there has been some difficulty in obtaining an oil with a specific gravity over 0.975. A good deal of this oil is now distilled in Spain, from which country some 50 tons are exported annually. According to Ménasché (*Perf. and Ess. Oil Record*, 1921, p. 149), the specific gravity of the genuine Spanish

\*From the *Pharm. Journ. and Pharm.*, August, 1921.

oil may be as low as 0.955. The limits given in the United States Pharmacopœia are 0.980 to 1.055 at 25°, and up to the last few years most commercial samples have fallen within these limits. It seems, however, that the minimum figure will have to be lowered. Possibly the variation is due to the method of distillation and the amount of tar present in the oil.

Genuine cade oil must be derived exclusively from the wood of *Juniperus oxycedrus* by dry distillation. *Juniperus oxycedrus* is a bushy shrub, differing from the other Juniper species by the simultaneous occurrence of needle-shaped leaves and of fruits which are orange-red when ripe. It grows on a chalky marly soil, and thrives best in a southern aspect. It occurs abundantly in the wild state in Provence and in the waste lands of Sommeres and Lussan. The woodcutters distinguish two kinds of wood, "cades gras" and "cades maigres"; only the former is used for distillation, the latter serving as fuel. The heart-wood is richest in oil, and the oil-content is said to increase towards the roots. For the purpose of distillation the bark is removed and the wood is then cut as small as possible. The preparation of the wood is very important, as the yield of oil is much greater from shavings than from larger chips. The distillation is carried on throughout the year, but preferably from September to May.

According to Pépin ("Recherches sur l'Huile de Cade Vraie," Paris, 1908) the oil is obtained by two methods in France—"distillatio per descensum" and by "combustion en milieu confiné." The former method is used only in the manufacture on a small scale. A cast-iron boiler is filled with shavings, then turned upside down on to its cover or a hollowed-out stone slab, and cemented up. In the centre of the bottom is a hole, which is connected with a delivery tube. A brisk fire is lighted so that the boiler is surrounded by the flames. Distillation commences with evolution of thick vapors, and soon afterwards a blackish viscid liquid flows off. The process lasts from half an hour to several hours, according to the quantity of wood. In place of a boiler a pit is sometimes used, with a stone slab at the bottom provided with a delivery pipe. The chips are heaped up in the centre of the cavity and covered over with bricks, which are luted together with clay. The rest of the pit is used for firing material.

The second process, that of incomplete combustion with exclusion of air, is used for production on a large scale. For this purpose a brick kiln is employed, 18 feet to 22 feet long and about 6 feet high, with an inclined bottom provided with a gutter, which allows the oil to drain into a vessel placed in a pit in front of the exit. The kiln is covered with earth except at the place where the cavity is, and for the purpose of filling it up with wood and setting fire to the latter, large openings are provided at the top and sides. After the fire is lighted these openings are closed, and distillation proceeds with simultaneous carbonization of the wood. The distillation frequently lasts several days. When the fire is too hot the resulting oil is more viscid and blacker than under normal conditions when the color is reddish-brown. The fresh distillate is left standing for two or three weeks, when it separates into three layers, of which the upper one is the oil of cade, the next is water, and the lowest consists of tarry products. Such methods of preparation must necessarily lead to variation in the character of the product.

According to Pépin, the specific gravity lies a little below 1.000; it makes a clear solution with 8 to 10 volumes of 96 per cent. alcohol, and in all proportions with ether, amyl alcohol, chloroform, acetic acid and benzene. The water-soluble acid-content should not exceed 1.5 per cent. calculated as acetic acid. When distilled at ordinary atmospheric pressure the fraction boiling between 150° and 300° should amount to 68 to 80 per cent., whilst pine tar yields only 15 per cent. between these temperatures. For the detection of pine tar oil the best test is the copper acetate reaction. One cc. of the oil is shaken with 15 cc. of petroleum ether and the mixture is then filtered. To 10 cc. of the filtrate an equal volume of a 5 per cent. solution of copper acetate is added and well shaken, 5 cc. of the petroleum ether layer is diluted with 10 cc. of ether and filtered. In the presence of pine tar oil the filtrate has an intense green color, whilst pure cade oil gives a chestnut-brown color.

Cade oil of Spanish origin, though of low specific gravity, contains a high proportion of cadinene, as shown by fractionation, and does not give a reaction for pine tar. It is guaranteed to be derived from *Juniperus oxycedrus*, and may, therefore, be accepted as genuine cade oil. The extreme limits for specific gravity I have observed for this oil during the last twenty years are 0.955 and 1.064.

## VITAMINES AND THEIR DISTRIBUTION.\*

Two years ago a report was published by a committee appointed jointly by the Lister Institute and the Medical Research Committee, detailing briefly "The Present State of Knowledge Concerning Accessory Food Factors (Vitamines)." The findings of this committee are of great interest. At the end of the report a valuable table is given, showing the distribution of the three vitamins in the commoner foodstuffs. In the absence of quantitative data it was impossible for the committee to do more than indicate the relative values of the foodstuffs as sources of the various vitamins, by the rough method of positive and negatives signs. The table, with slight modifications, follows:

<i>Classes of Foodstuff.</i>	<i>Fat-Soluble A or Anti- rachitic Factor.</i>	<i>Water- Soluble B or Antineuritic (Antiberi- beri) Factor.</i>	<i>Antiscor- butic Factor.</i>
<i>Fats and Oils:</i>			
Butter .....	+ + +		
Cream .....	+ +		
Cod-liver oil .....	+ + +		
Mutton fat .....	+ +		
Beef fat or suet .....	+ +		
Peanut oil .....	+		
Fish oil, whale oil, etc. ....	+ +		
Margarin prepared from animal fat .....	Value in pro- portion to amount of animal fat contained		
	+		
Nut butters .....	+		
<i>Meat, Fish, etc.:</i>			
Lean meat (beef, mutton, etc.)..	+	+	+
Liver .....	+ +	+ +	+
Kidneys .....	+ +	+	
Heart .....	+ +	+	
Brain .....	+	+ +	
Sweetbreads .....	+	+ +	
Fish, white .....	..... very slight, if any		
Fish, fat (salmon, herring, etc.)	+ +	very slight, if any	
Fish, roe .....	+	+ +	
Canned meats .....	?	very slight	

\*From the *Journ. of the A. M. A.* August, 1921.

<i>Classes of Foodstuff.</i>	<i>Fat-Soluble A or Anti- rachitic Factor.</i>	<i>Water- Soluble B or Antineuritic (Antiberi- beri) Factor.</i>	<i>Antiscor- butic Factor.</i>
<i>Milk, Cheese, etc.:</i>			
Milk, cow's whole, raw .....	+	+	+
Milk, skim, raw .....		+	+
Milk, dried, whole .....	less than +	+	less than +
Milk, boiled, whole .....	undetermined	+	less than +
Milk, condensed, sweetened ....	+	+	less than +
Cheese, whole milk .....	+		
<i>Eggs:</i>			
Fresh .....	+	+	?
Dried .....	+	+	?
<i>Cereals, Pulses, etc.:</i>			
Wheat, maize, rice, whole grain.	+	+	
Wheat germ .....	+	+	
Wheat, maize, bran .....		+	
Linseed, millet .....	+	+	
Dried peas, lentils, etc. ....		+	
Soy beans, haricot beans .....	+	+	
Germinated pulses or cereals ...	+	+	+
<i>Vegetables and Fruits:</i>			
Cabbage, fresh (raw) .....	+	+	+
Cabbage, fresh (cooked) .....		+	+
Cabbage, dried .....	+	+	very slight
Cabbage, canned .....			very slight
Swede (rutabaga) raw ex- pressed juice .....			+
Lettuce .....	+	+	
Spinach (dried) .....	+	+	
Carrots, fresh, raw .....	+	+	+
Carrots, dried .....	very slight		
Beetroot, raw, expressed juice..			less than +
Potatoes, raw .....	+	+	
Potatoes, cooked ..			+
Beans, fresh, scarlet runners, raw .....			+
Onions cooked .....			+
Lemon juice, fresh ..			+
Lemon juice, preserved .....			+
Lime juice, fresh .....			+
Lime juice, preserved .....			very slight
Orange juice fresh ..			+
Raspberries .....			+
Apples .....			+
Bananas .....	+	+	very slight
Tomatoes (canned) .....			+
Nuts .....	+	+	



<i>Classes of Foodstuff.</i>	<i>Fat-Soluble A or Anti- rachitic Factor.</i>	<i>Water- Soluble B or Antineuritic (Antiberi- beri) Factor.</i>	<i>Antiscor- butic Factor.</i>
<i>Miscellaneous:</i>			
Yeast, dried .....	.....	+ + +	
Yeast extract and autolized ....	?	+ + +	
Malt extract .....	.....	+ in some specimens	

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None of the three factors were found in:

Lard.

Olive, cottonseed, coconut or linseed oils.

Coco butter.

Hardened fats, animal or vegetable in origin.

Margarin from vegetable fats or lard.

Cheese from skim milk.

Polished rice, white wheaten flour, pure cornflour, etc.

Custard powders, egg substitutes, prepared from cereal products.

PeafLOUR (kilned).

Meat extract.

Beer.

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## THE CULTIVATION OF ERGOT.\*

Whether ergot can be successfully cultivated on a large scale is a question that has of late often been asked. The drug was formerly collected chiefly in Russia and Galicia; smaller quantities came from Spain and Algeria, but very little from Central and Western Europe. The present scarcity is due to the absence of supplies from Russia and Galicia, and as these countries will probably not export any for a considerable time, the conditions are favorable for the attempt at cultivation on a scale sufficiently large to allow of export.

The investigations of Tulasne and Kühn have made us familiar with the life-history of ergot. The sclerotium is developed in the summer in the inflorescence of certain Gramineaceous plants and replaces the ovary; when mature it falls to the ground, retaining its vitality until the following spring. Numbers of stromata with their characteristic spherical heads then develop from the sclerotium. In

\*Abstracted from "Die Kultur des Mutterkornes," by Prof. L. Hecke, Vienna (*Schweiz. Apoth. Ztg.*, 59, p. 277). Reprinted from *Pharm. Journ. and Pharm.*

warm weather the stromata ripen quickly, the color passing from yellow to violet; in them myriads of perithecia are formed, and in these the asci containing the very slender spores are developed. These spores are ejaculated from the perithecia, and, being carried by the gentlest currents in the atmosphere, are raised in the air and borne to the flowers, which must be open to receive them. A single spore entering an open flower and resting on the ovary is sufficient to cause the infection. The spore develops, the ovary perishes, and its place is taken by a whitish, cheesy mass of mycelium which, in about eight days, forms multitudes of conidia and simultaneously secretes a viscous, sweet honey-dew, the "sphacelia segetum" of the older authorities. This is visited by various insects (*Melanostoma mellina*, *Rhagonycha fulva*, *Sciara Thomæ*, etc.), and the honey-dew, with the conidia suspended in it, is carried to other plants where further infection is effected, provided, of course, that open flowers are still present. The sphacelia gradually hardens to a sclerotium, on the apex of which its remains are often to be found in the form of a whitish cap (still containing conidia).

Ergot occurs not only on rye, but also, though less frequently, on barley, rarely on wheat, but often on a large number of wild grasses, *e. g.*, *Anthoxanthum*, *Arrhenatarum*, *Dactylis*, *Festuca*, *Phalaris*, *Briza*, *Calamagrosti*, etc. On other grasses special forms may occur which will not develop on rye; for example, a form is found on *Lolium perenne*, which will not develop on rye, but which can pass to *Bromus*, *Molinia*, and other grasses.

Rye is the only host practically available for the cultivation of ergot, but it is hopeless to expect success from sowing ergots in a rye field. This has been tried and has failed. Infection depends on so many circumstances that the quantity of ergot produced may easily be less than the quantity sown. In the most favorable instances barely one per cent. of the grain harvested will be ergot. The infection must be artificial. The sclerotium is necessarily the starting-point, and it must be induced to germinate at the right time, for if the discharge of the spores does not coincide with the flowering of the rye no infection can take place. The conditions of germination must therefore be accurately known. Ergots will not germinate satisfactorily unless they have wintered in the open; if kept in a room and then sown in the spring they will germinate either badly or not at all. Probably the frost has some action on the sclerotium

as it has in the case of the teleutospores of certain russ. A rest period appears to be necessary, but its length is unknown.

As far as is at present known, ergots are best germinated by sowing them about one centimeter deep in boxes of sandy earth in the autumn, and then sinking the boxes in the open ground. They will then germinate with perfect regularity in the spring, when the weather is warm and moist. If necessary the boxes may be covered with glass. Sclerotia that have been made capable of germination by exposure to frost can be taken up in February and kept dry till wanted. Rapidity of germination appears to depend chiefly on the temperature; at ordinary room temperature the first stromata will appear in about a fortnight. The ejaculation of the spores can easily be observed under a strong lens; it lasts at least several days, and is influenced by warmth and moisture; it may even cease and then recommence. Although the number of spores ejaculated from each head is very large, their direct utilization for the purpose of infection is not feasible. The sphacelia with its conidia is much better adapted for this purpose. Large quantities can be produced either on the rye grain itself or by means of a pure culture. In the former case several inflorescences are enclosed in glass tubes closed at each end with cotton, wool, and ergots with ripe asci are introduced. As the flowers open they become infected and produce honey-dew in about eight days; this can be collected, suspended in water, and the suspension used in a spray for infection on a large scale. This method is attended by numerous practical difficulties, and it is preferable to obtain the quantity of sphacelia necessary by pure culture. This is easily done by allowing the spores to be ejaculated from the perithecia on to nutrient gelatin in Petri dishes. The spores germinate at once, and the colonies can be transferred, together with a small piece of the gelatin, to a suitable nutrient medium contained in large flasks. In these enormous quantities of conidia are produced. Further propagation by inoculation is easy, so that there is no difficulty in having the necessary amount always at hand. As the sclerotia can be induced to germinate during the winter the cultivation of the sphacelia can be carried on during the spring at a time convenient for the flowering of the rye. The cultures are shaken with water, and the suspension used with a spray.

Infection is very difficult. It can be accomplished only when

the flower is open, and is, therefore, practically confined to such flowers as open and are subject to cross-fertilization. Barley and wheat are seldom attacked, as they are self-fertilized, and the flowers do not open. Rye is usually cross-fertilized, the self-fertilized flowers being sterile; the flowers open when the anthers are ripe. The time during which the flower remains open depends on the time at which fertilization is effected, and varies. Isolated rye plants by the wayside or scattered in fields of wheat where the prospects of fertilization are small may keep their flowers open for a week, and these are the plants that are most commonly infected by ergot. In the case of fields of rye in which clouds of pollen are produced fertilization is quickly effected and the flowers close. The flowering of a field of rye is over in about a week; this is about the time the sphacelia takes to develop after the spore has attacked the ovary. The conidia produced by the sphacelia, therefore, finds no flowers open and ready for infection, and this method of the further dissemination of the ergot is not available. In the cultivation of ergot the endeavor must accordingly be made to hinder the fertilization as much as possible, and so prolong the period of flowering. With this object in view, the rye should not be sown in fields, but in single rows between rows of other plants, such as maize. Damp, windless weather is unfavorable for fertilization, and, therefore, favorable for the dissemination of the ergot. Sites for the cultivation of ergot should be sought in damp localities where the air is still.

Another method of prolonging the time during which the open flowers are available is by sowing at intervals of a week or fortnight. The plants should be about ten centimeters apart, so as to favor the development of several stems with inflorescences developing at different times. Special species or varieties, such as *secale montanum*, may also be sown. By such means the duration of the flowering may be extended from the middle of June to the end of September.

The cultivator visits the plants daily, or more than once a day, and sprays the open flowers with conidia suspension. Once infection is effected, further dissemination is carried out by natural means. There is no doubt that the cultivation on a large scale is feasible, but it must be carried out by specially trained workers. The danger of infecting rye fields in the neighborhood of the cultivation is

small, and a distance of 100 meters would probably be sufficient to ensure safety, particularly if the cultivation is carried out with late-flowering species.

Experiments are now in progress with the view of ascertaining whether the cultivation is likely to be financially successful.

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## SCIENTIFIC AND TECHNICAL ABSTRACTS

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HYDROGEN PEROXIDE; DETECTION AND DETERMINATION OF TRACES OF —. F. W. Horst. *Chem.-Zeit.*, 1921, 45, 572.—Traces of hydrogen peroxide may be determined qualitatively and quantitatively by reduction with ferrous sulphate, and colorimetric estimation of the ferric sulphate formed by means of ammonium thiocyanate. The ferrous sulphate solution must be freed from traces of ferric salt by passing hydrogen sulphide through it, first in the cold and then at the boiling point, and is cooled in a current of carbon dioxide. Twenty cc. of the sample to be tested is placed in a graduated tube, and a few cc. of petroleum spirit is added as a protection against oxidation during the reaction. About 2 cc. of the ferrous sulphate solution is added and agitated with the sample by means of a current of carbon dioxide. Five cc. of air-free ammonium thiocyanate solution is then introduced, and the color is compared with that of a standard solution.—W. J. W., through *Journ. of Soc. of Chem. Ind.*

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AMMONIUM SULPHATE AS A WEED KILLER.—Reporting on sulphate of ammonia as a weed-killer, the Experimental Station of the Rhode Island State College says that this method of reducing or eliminating weeds from lawns was developed there by a series of experiments extending over twenty years. All lawn grasses require in order to grow at their best that the soil be supplied with plenty of plant food in the three elements found in commercial fertilizers—nitrogen, phosphorus and potassium. Most grasses and weeds also require that the soil be not sour; but some kinds which make an even turf grow well in an acid soil. The usual fertilizers employed

for top-dressing lawns in the spring do not develop acidity, and permit the coarsely growing weeds to crowd out the grass. Nitrogen is commonly furnished in nitrate of soda, which tends towards an alkaline reaction. By substituting a similar amount of sulphate of ammonia, which is not more expensive, an acid condition of the soil is gradually produced which weakens the weeds, while not affecting the special grasses referred to—bent Grasses or Fescues. Thus in two or three seasons the weeds will entirely disappear, or in new lawns will never become troublesome. The phosphorus can be applied in acid phosphate, and the potash in muriate of potash, as usual. Different soils require different amounts of plant food; but a good proportion for average conditions is 250 pounds of sulphate of ammonia, 400 pounds of acid phosphate, and 250 pounds of muriate of potash to the acre. A smaller quantity than this should be used on newly-seeded lawns. A too heavy application of sulphate of ammonia will injure the grass as well as the weeds; but in the proportion noted it may safely be used as freely as the common lawn fertilizers. It is necessary that the fertilizer be distributed evenly when the lawn is dry, in order not to burn the grass; and where convenient it is well to sprinkle the lawn thoroughly after applying the fertilizer.—*Gas Journal*, through *Chem. Trade Journ.*, July 30, 1921, 128.

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AN IDEAL ZINC OINTMENT.—Mr. A. H. Clark, of the School of Pharmacy, University of Illinois, read a paper before the American Pharmaceutical Association on the best formula for zinc ointment from the standpoints of therapeutic activity and keeping qualities. He found that an ointment made with lard produces a disagreeable odor and becomes granular. With lanoline and yellow soft paraffin an unpleasant odor develops. White wax gives an ointment that is very liable to shrink. The ideal ointment is obtained with the following formula:

Soft white paraffin .....	65 parts
Hard paraffin .....	15 parts
Zinc oxide .....	20 parts

This ointment is odorless, does not shrink, nor does it separate or granulate.

OIL OF WILD PIMENTO LEAVES.—According to Roberts ("J. S. C. I.," 1921, 40, 94) the essential oil distilled from the leaves of *Amomis jamaicensis* contains 17 per cent. of terpenes, including dipentene and  $\alpha$ -phellandrene, 15 per cent. of eucalyptol, traces of aldehydes, 38.3 per cent. of alcohols, principally *l*-linalol with some geraniol, 1.5 per cent. of linalyl acetate, and traces of phenols and free acids. Sesquiterpenes are also probably present.—Through the *Chem. & Druggist*.

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ESSENTIAL OIL OF JUNIPERUS TAXIFOLIA.—Shinosaki (*Journ. Chem. Ind., Japan*, 1921, 24, 202) has obtained 0.24 per cent. of a pale green oil by distillation of the leaves and twigs of *Juniperus taxifolia*, a coniferous plant growing in the Ogasawara Islands. The oil contains about 50 per cent. of  $\alpha$ -pinene, in both the dextro-rotatory and the levorotatory varieties. A second terpene, apparently bicyclic, is present, a free alcohol of the formula  $C_{10}H_{18}O$ , an ester, a sesquiterpene, and a sesquiterpene alcohol.—Through the *Chem. & Druggist*.

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SIAM BENZOIN.—Reinitzer (*Arch. Pharm.*, 1921, 259-60) publishes further details of his investigation of the constituents of Siam benzoïn. Lubanol benzoate  $C_{17}H_{16}O_4$  crystallizes in plates melting at  $72^{\circ}$ - $73^{\circ}$ . It becomes oxidized by exposure to the air, and then exhibits the series of color changes which are identical with those shown by the crude gum resin itself. On heating, it evolves benzoïc acid, and then gives off an odor of carnations, and eventually of guaiacol. It is believed that lubanol is either identical with, or closely related to, coniferyl alcohol. This point can only be decided when pure lubanol itself is obtained in the crystalline condition.—Through the *Chem. & Druggist*.

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OIL OF ERGOT.—A freshly-gathered sample of ergot from Obersteiermark yielded only 21 per cent. of oil on extraction with petroleum ether, the saponification value of which was 196.2, as compared with the only previously recorded figure of 180. The neutralization value of the insoluble fatty acids, 194.8, and the acetyl saponification value, 248.7, were similar to those of a sample that had been kept for ten years. The acetyl value, 86.6, was, however, higher in

the case of the fresh oil. The melting point of the fatty acids was  $39.5^{\circ}$  C., and the solidifying-point  $38.6^{\circ}$ - $36.5^{\circ}$  C. by the capillary method.—K. Gander and J. Zellner (*Seife*, 1921, 6, 411, through *Journ. Soc. Chem. Ind.*, July 30, 1921, 518A).

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MANUFACTURE OF LUMINOUS PAINTS.—Four methods for the manufacture of phosphorescent pigments are described. The first utilizes oyster shells as the raw material. The shells are first washed with hot water and then dried and calcined at a bright red heat. After cooling, the mass is crushed and freed from the *débris* of the external layers, which is valueless for the purpose in hand. The shell powder is then mixed with a small amount of powdered wood charcoal and transferred to a crucible made of a refractory earth, where it is arranged in alternate layers with powdered sulphur. The crucible, covered by a lid securely luted on, is strongly heated for about an hour, and after complete cooling the mass is extracted and pulverized once again. A phosphorescent color prepared in this way from an impure carbonate of lime possesses a more intense lustre than the colors made from pure carbonate of lime. In the second method the sulphates of calcium, barium, or strontium are used as the raw materials. These are intimately mixed with powdered wood charcoal, in the proportions of 1 part of carbon to 5 or 6 parts of sulphate. The mixture is then calcined as in the previous process. In the third method, when working with carbonates such as marble, witherite, or carbonate of strontium it is necessary to add, in addition to the wood charcoal, rather more than one chemical equivalent of sulphur, and then to proceed in the same manner as with the oyster shells. The second and third processes give masses with an orange, green, blue or red phosphorescence. The sulphur is sometimes replaced by antimony sulphide or other similar sulphur compounds. More luminous but more expensive colors can be produced by starting with calcium oxide, barium carbonate, or carbonate or sulphate of strontium, either alone or mixed with calcium oxide or marble. The necessary carbon is obtained from starch, which is mixed with the above substances. The carbonates of rubidium and lithium, as well as bismuth nitrate, are equally of service. Sometimes sodium sulphate, or even lead acetate, is added, and the formulæ for the mixings vary with each individual factory. It may be



taken as a general rule, however, that about 80 parts of the principal constituent require 12 parts of sulphur (or less if other sulphur compounds be present); 4 to 5 parts of starch, 2 to 4 parts of lithium carbonate, and 0.01 to 0.5 part of other metallic compounds. Those constituents, which are used only in very small amounts, are best added in alcoholic solution. The mixtures are heated in a hermetically sealed crucible for three-quarters to one hour at a temperature of about 1200° C. Phosphorescent pigments are, when used, often mixed with barium sulphate, lakes of natural coloring matters, and often with mineral pigments of the same shade as the phosphorescent body itself. Thus, for example, realgar is used with red shades and orpiment with yellow shades.—O. Prager (*Chem. Tech. Fabrikant*, through *Chem. Trade Journ.*, August 6, 1921, 158).

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ALKALOIDS OF VALERIAN.—Goris and Vischniac (*Répert. de Pharm.*, June 6, 1921) extracted 5 kilos. of an aqueous extract of valerian, representing 40 kilos. of fresh root, with a 10 per cent. solution of sodium carbonate, treating the liquid with a mixture of ether and chloroform, then with water containing 2 per cent. of hydrochloric acid, finally saturating this solution with carbonate of potassium, and successively extracting with ether and with chloroform. They succeeded in obtaining 4 gm. of crude bases, from which they were able to separate 3 gm. of chantinine and 1 gm. of valerine. The former is difficult to obtain in a crystalline form, except as the picrate, which melts at 97° to 98°. Animal experiments showed that these two alkaloids have practically no physiological action; the therapeutic properties of valerian are therefore not due to these two bodies.—Through the *Chemist & Druggist*.

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SACCHARIN REACTION.—L. Thevenon, a pharmacist in Oullins, describes a new reaction of saccharin (*Jour. Pharm. Chim.*, No. 11, 1920). On adding 10 cc. of a solution of 0.1 gram of sodium nitrite in 100 cc. of distilled water, and six drops of sulphuric acid (1/3), to a solution containing 0.1 gram of saccharin in 25 cc. of distilled water, the further addition of 0.1 gram of beta-naphthol to the mixture causes the immediate production of an intense red coloration, which may be fixed to wool and silk, and is permanent.

It is sufficiently sensitive to detect traces of saccharin in foodstuffs, after extraction by alcohol and water in the usual way, preferably adding the sulphuric acid to the solvent employed for extraction.—Through the *Chemist & Druggist*.

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A NEW METHOD FOR THE ESTIMATION OF MORPHINE.—Trifon Ugarte (*Journ. de Pharm. et de Chim.*, February 16, 1921). One gram of powdered opium is introduced into a flask of 200 cc. capacity, and 10 cc. of alcohol (67 per cent.) is added. The mixture is placed on the water bath for five minutes, and then filtered. The filtrate is collected in a crystallizing pan with a diameter of 7 centimetres and 2 centimetres deep. The insoluble portion is treated successively three times as described, and the filtrates collected in the crystallizing pan. The collected liquids are evaporated on the water bath, and the dry residue is maintained for 15 minutes at a temperature of 100°, to oxidize the resins, and thereby render them insoluble; 5 cc. of cold distilled water is now added to the residue and filtered into a flask having a capacity of 200 cc. This operation is repeated three times, and the collected 20 cc. of liquid is evaporated on the water bath. The residue is dissolved in 2 cc. of water saturated with morphine, and under agitation 3 cc. of normal solution of ammonia saturated with morphine are added, as well as 10 cc. of ether, and the whole shaken. The shaking causes a rapid fall in temperature, due to the evaporation of the ether. A further addition of 20 cc. of ether is made, and the mixture set aside for 30 minutes. The morphine now crystallizes out in the form of small granules. After adding 10 cc. of ether the mixture is filtered, the crystals of morphine are removed by means of a glass rod provided with an India rubber cap, and by the use of a jet of distilled water saturated with morphine and ether. The filters are then dried at a temperature of 100° to 105° and weighed.—Through the *Chemist & Druggist*.

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THE EFFECT OF ALKALINITY ON THE USE OF HYPOCHLORITES.—E. K. Rideal and W. R. Evans, in the *Journal of the Society of Chemical Industry*, point out that the keeping qualities of solutions of hypochlorites are enhanced by the presence of free alkali, but that when used as disinfectants or for treatment of water to destroy

organisms, they act more efficiently when acid; in fact, the oxidizing power of these solutions is greatly depressed by the presence of alkali. They suggest for treatment of alkaline waters the simultaneous addition of nitre cake.

The variability of chlorinated lime—as it reaches the consumer—appears to have considerable public importance. One sample (packed in paper) purchased at a local store was found to contain only traces of available chlorine. The unstable character of chlorinated lime—even at low temperatures—is little appreciated. It decomposes very rapidly if exposed to damp air or to carbon dioxide. Solution of sodium hypochlorite keeps much more satisfactorily, so long as it is kept in a cool place, protected from light and from access to carbon dioxide.—J. S. C. I., Feb. 28, 1921.—Through the *Aust. Journ. of Pharm.*

APPROXIMATE ESTIMATION OF COMMERCIAL CRESOL IN LYSOL. C. J. Jordan and F. Southerden. (*Pharm. J.*, 1921, 106, 479-480.)—Products of somewhat varied composition are sold under the name "lysol," but most of them consist essentially of a strong solution of castor oil or linseed oil soap incorporated with commercial cresol. To estimate the amount of cresol present 60 gm. of the sample is acidified with 30 cc. of dilute sulphuric acid and steam-distilled until the distillate no longer gives a blue coloration with ferric chloride. The whole distillate is shaken thoroughly, but not too violently, so as to ensure saturation of the aqueous layer, and then set aside for a few hours. The volume of the cresol layer multiplied by 1.04 and added to one-fiftieth of the volume of the aqueous layer gives the weight of cresol in the portion of the sample taken. The method yielded trustworthy results in the case of mixtures containing known amounts of cresol. It is generally agreed that "lysol" should contain 50 per cent. of cresol, but analyses of ten different brands showed that in some cases the cresol content was about 40 per cent., and in one sample 35 per cent.—W. P. S., through *The Analyst*, Sept., 1921.

MITRAGYNINE AND MITRAVERSINE, TWO NEW ALKALOIDS FROM SPECIES OF MITRAGYNE. E. Field. Chem. Soc. Trans., 1921, 119, 887-891.—The residue obtained by evaporating the alcoholic ex-

tract of the leaves of *Mitragyne speciosa* (N. O. *Rubiaceæ*) when dissolved in glacial acetic acid, freed from chlorophyll and resin by addition of water, and made alkaline with ammonia, yields an amorphous precipitate, which when dissolved in 20% acetic acid and treated with a hot aqueous solution of picric acid yields a crude picrate,  $C_{22}H_{31}O_5N.C_6H_3O_7N_3$ , orange-red needles from methyl alcohol, m.p.  $223^{\circ}$ — $224^{\circ}$  C., representing 0.3% of the initial weight of the leaves. The free alkaloid is obtained by dissolving the picrate in boiling glacial acetic acid and pouring into dilute ammonia, filtering while hot. The new alkaloid, for which the name mitragynine is suggested, is a colorless amorphous solid, m. p.  $102^{\circ}$ — $106^{\circ}$  C., distilling unchanged at  $230^{\circ}$ — $240^{\circ}$  (5 mm.); it contains three methoxy groups, but no N-methyl groups, and is probably  $C_{17}H_{22}N(OCH_3)(CO_2CH_3)_2$ . Hydrolysis with sodium ethoxide gives a dicarboxylic acid, m.p.  $280^{\circ}$ . Both this acid and alkaloid give the indole reaction with hydrochloric acid and vanillin. The acetate, mono- and trichloro-acetates, and the hydrochloride are described. Similar treatment of the leaves of *M. diversifolia* gives an alkaloid, for which the name mitraversine is suggested, having m. p.  $237^{\circ}$  C. molecular weight 328, and containing 2 methoxy groups. The hydrochloride melts at  $208^{\circ}$ — $210^{\circ}$ . It is probably  $C_{22}H_{26}O_4N_2$ .—P. V. M., through *Journ. of Soc. of Chem. Ind*

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## NEWS ITEMS AND PERSONAL NOTES

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FREE PUBLIC LECTURE COURSE, 1921-1922, PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE, 145 NORTH TENTH STREET.

First Lecture. Thursday evening, October 6, 1921. "The Chemistry of Other Worlds." By Prof. Henry Leffmann, A. M., M. D., Lecturer on Research, Philadelphia College of Pharmacy and Science; Hon. Prof. Organic Chemistry, Wagner Free Institute of Science, etc.

Modern astronomy, especially by the aid of photography, has enabled us to obtain much information about the physical and chemical nature of the heavenly bodies. In addition to the members of our own system—sun, moon and planets—immense numbers of fixed stars exist, which with comets, nebulae and meteors, have furnished

additional facts. It appears that the forms and compositions of all these bodies are much like those of our own planet, but peculiar conditions are occasionally found. One remarkable incident was the finding of an element in the sun before it was known to exist on the earth, and the subsequent discovery of it in certain parts of the United States in amounts sufficient to make it available for war purposes. This lecture will present, vividly, by lantern slides, many interesting facts concerning the form and nature of the heavenly bodies, and incidentally discuss the possibility of the existence of intelligent beings on other worlds.

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Second Lecture. Thursday evening, October 20, 1921. "Petroleum and Its Products and Their Modern Uses." By Prof. F. P. Stroup, Ph. M., Professor of Chemistry, Philadelphia College of Pharmacy and Science.

A brief resume of the occurrence, methods of production and refining of petroleum, and a discussion of the properties and uses of its products, with special reference to motor fuels. Illustrated with lantern slides and specimens and a working model of oil well machinery.

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Third Lecture. Thursday evening, November 10, 1921. "Products From Cotton Fields and Forests." By Prof. J. W. Sturmer, Phar. D., Professor of Pharmaceutical Chemistry, Lecturer on Industrial Chemistry, Philadelphia College of Pharmacy and Science."

The industries based upon the chemical utilization of cellulose, the substance which constitutes cotton fiber and which may be separated also from wood pulp, are of increasing importance. Varnishes, artificial leather, artificial silk, celluloid, paper of all description and kinds, paper clothes, and scores of other products, are manufactured in great quantities. The lecture, which will be illustrated, will deal with the newer aspects of this subject.

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Fourth Lecture, Thursday evening, November 17, 1921. "Strawberries at the North Pole and Apples at the Equator." By Prof. Heber W. Youngken, A. M., Ph. D., Professor of Botany and Pharmacognosy, Philadelphia College of Pharmacy and Science.

An exposition of the recent methods of dehydration as employed for the preservation of foods of various classes. The ad-

vantages of these methods over desiccation, evaporation, cold storage, heat and chemical processes. This lecture will be illustrated with a variety of dehydrated products.

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Fifth Lecture. Thursday evening, December 15, 1921. "Our Bacterial Friends and Enemies (The One Class to Be Protected and the Other Destroyed)." By Prof. Louis Gershenfeld, B. Sc., Professor of Bacteriology, Philadelphia College of Pharmacy and Science.

The micro-organisms—their discovery and classification. Development and scope of bacteriology. The general characteristics and activities of bacteria. Their relation to health and disease. Bacteria in humans and animals, air and soil, drinks and foodstuffs. Bacteria of value and harmful in the arts and industries.

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Sixth Lecture. Thursday evening, January 5, 1922. "Chemistry in Peace and War." By Prof. P. Fischelis, B. Sc., Phar. D., Consulting Chemist, Member Editorial Staff, *The Journal of Industrial and Engineering Chemistry*; Dean of the New Jersey College of Pharmacy.

The dependence of America in peace-time pursuits and the possibility of transforming these industries, when necessary into factories for producing engines of destruction, poisonous gases and high explosives.

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Seventh Lecture. Thursday evening, January 19, 1922. "A Thousand and One Odors" (Of interest to those who use perfumery and those who desire to make it). By Prof. E. F. Cook, Ph. M., Director of the Pharmaceutical Laboratory, Philadelphia College of Pharmacy and Science.

First Part. A popular presentation of the history of perfumery with a description and samples of those materials from material sources which the perfumer can utilize and a brief, illustrated story of their production and marketable forms.

Second Part. An account of the synthetic production of perfumes, their chemical character and a display of samples of the artificially produced flower odors.

Third Part. A display of modern perfumes and perfumed products.

Eighth Lecture. Thursday evening, February 2, 1922. "Standardized Remedies" (How they conserve life and what the public should know about them, including the newer serums and vaccines). By Prof. Paul S. Pittenger, B. Sc., Lecturer on Physiological Assaying, Philadelphia College of Pharmacy and Science.

How drugs are tested for strength and value by modern scientific methods, including a brief description of some of the newer biological remedies, such as serums, vaccines, etc.

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Ninth Lecture. Thursday evening, February 16, 1922. "How Chemistry Develops the Industries" (Of particular appeal to men and women who wish to apply chemistry in manufacturing). By Prof. Frank X. Moerk, Ph. M., Director of the Chemical Laboratory, Philadelphia College of Pharmacy and Science.

Examination of raw materials and final products; increased production; utilization of waste products. Rapid methods of examination.

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Tenth Lecture. Thursday evening, March 2, 1922. "One Drop of Blood" (The story of health and sickness told in a most fascinating way). By Ivor Griffith, P. D., Ph. M., Serologist and Clinical Chemist, Stetson Hospital, Philadelphia, Editor *American Journal of Pharmacy*; Instructor in Pharmacy, Philadelphia College of Pharmacy and Science.

Its constituents, its role in health and sickness. The mechanism of coagulation. Its changes in disease. Its constant defensive warfare. Invasion of bacterial hordes. The summoning of the great white hosts, their mode and instruments of warfare, the hidden hormones, the unknown enzymes, and the subtle platelets. The bacteria are overcome and cannibalized and the disease conquered, the day is won and life persists.

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Eleventh Lecture. Thursday evening, March 16, 1922. "The Foods of the Next Century." By Prof. Chas. H. LaWall, Ph. M., Sc. D., Chemist to Food Bureau, Pennsylvania Department of Agriculture; Professor of Pharmacy, Philadelphia College of Pharmacy and Science.

A brief historical survey of foods with particular reference to new and interesting foods of the present and the probable development of the future in this interesting and important field.

Twelfth Lecture. Thursday evening, April 5, 1922. "The Raw Materials of the Chemical Industry." By Prof. Samuel P. Sadtler, Professor Emeritus of Chemistry, Philadelphia College of Pharmacy and Science.

The successful development and establishment of a chemical industry is primarily based upon a supply of cheap and satisfactory raw materials.

For the inorganic chemical industries these are:

Fuels, including coal, petroleum oil and natural gas; salt, either solid or in the form of brine, limestone; sulphur or pyrites; phosphates; nitrates.

For organic industries:

Fuel, as before stated; wood and cellulose fibre; other textile fibres; sugar and starch yielding raw materials.

Review of the position of the United States in respect to these materials.

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Thirteenth Lecture. Thursday evening, April 29, 1922. "Food From the Air." By Dr. Henry Leffmann, A. M., M. D.

A popular and interesting account of how the nitrogen of the air can be made to enter into such combinations as make it available for many industrial and commercial processes. The newer work on the up-building of proteins makes it possible to expect a food supply from the air at some not far distant date.

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Fourteenth Lecture. Thursday evening, May 4, 1922. "Natural Silk and Artificial Silk." By Dr. Chas. E. Vanderkleed, Lecturer on Chemical Control, Philadelphia College of Pharmacy and Science; During the World War With Hercules Powder Company.

Comparisons and contrasts between natural silk and artificial silk. Methods of preparation of natural silk and of manufacture of artificial silk. Commercial uses and possibilities of both varieties.

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DR. JOSEPH JACOBS, OF ATLANTA, GEORGIA, IS HONORED BY THE UNIVERSITY OF GEORGIA.—A recent issue of the *Atlanta Georgian* carries the following report of honors bestowed upon Dr. Jacobs, a



loyal member of the Philadelphia College of Pharmacy and Science, and an earnest worker in the ranks of pharmacy:

"Thousands of Georgians will heartily indorse the action of the University of Georgia in bestowing the honorary degree of doctor of science on Dr. Joseph Jacobs, a loyal alumnus of the university and scholar who has conferred distinction on his Alma Mater by his distinguished achievements in science during his professional career.

"Doctor Jacobs, who was a member of the Class of 1879 and was a pupil of Dr. Crawford W. Long, has devoted many years to the development in pharmaceutical use of plants indigenous to the South and it was because of the importance of that work, as well as his literary work and research in establishing beyond a doubt the priority of Dr. Crawford Long's discovery of ether-anesthesia that he was given the honorary degree.

"One of the features of the commencement season at Athens this year was the unveiling of the medallion in memory of Dr. Crawford W. Long, presented by Doctor Jacobs.

"Doctor Jacobs also authorized the trustees of the university to offer in his name \$50 in gold as an annual prize for the best paper submitted by a student on Doctor Long and his discovery of anæsthesia.

"After the unveiling of the medallion to Doctor Long, the three daughters of the great discoverer presented to Doctor Jacobs an oil painting of their father.

"In presenting the monument and medallion to the university, Dr. Jacobs made an address in which he spoke of his association with Dr. Long, and extolled the value to humanity of the discovery of ether anæsthesia.

"That I have been permitted to present this monument to the University of Georgia, and that her trustees have accorded me the honor of its acceptance,' declared Dr. Jacobs, 'fills my heart with sentiments of gratitude and pride.

"My early boyhood and all my adolescent years were spent in this good city of Athens, and of her I can truly say:

"Where e'er I've roamed, what other realms to see  
My heart untraveled, has fondly turned to thee."

"It was during those years of my life in Athens that Dr. Crawford W. Long, whose wonderful achievement we here commemorate, was my employer in pharmacy and my much respected tutor. The countless acts of friending by which he then benefited me, I have, in all the years, treasured in recollection with "miser care." And hence, in considering how I might in appropriate form attest some small measure of my apprecia-

tion of the man and his invaluable contribution to the welfare of humanity, I thought these shades in which he pursued his academic studies, here, at his alma mater—old Franklin College—the proper place for a record of its expression.

“Dr. Crawford W. Long was a graduate of this university of the Class of 1835. Although he completed a full medical course at the University of Pennsylvania, and benefited by practical experience in the hospitals of New York City, yet I have often thought that, from the spirit of the motto of our university, the spirit of research, “*et docere, et causas rerum exquirere*,” “both to teach and to seek out the causes of things,” he formed the habit of clear and patient observation of facts, which enabled him, in the exercise of his deeply humane and sympathetic nature, to make his unexcelled discovery, in the realms of the curative science, for which he will be known in all future time as the conqueror of surgical agony. The day, March 30, 1842, on which Dr. Crawford W. Long discovered ether anæsthesia will be known in the annals of the world as the day of the world’s most important medical discovery.

“May I not here recall the fact that after Congress passed the act establishing the National Hall of Fame at Washington, Georgia’s Legislature created a commission to select the names of those two Georgians whose statues should be placed in that hall. This commission met in our State library, July 1, 1902, and chose the names of Crawford W. Long and Alex. W. Stephens as those to be thus distinguished. May we not all hope that our next general assembly will provide the necessary appropriation for the execution and fulfillment of this work.

“Too long we have permitted our people and his daughters to say of Dr. Crawford W. Long:

“ “Though known to few, thy unrewarded fame was truly won,  
Some day thy nation’s heart shall proudly claim her gifted son.”

“ ‘Mr. Chairman, it affords me great pleasure to tender this monument and medallion to the University of Georgia.’ ”

# THE AMERICAN JOURNAL OF PHARMACY

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## EDITORIAL

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### THE DAWN OF A NEW ERA IN SCIENTIFIC PHARMACY.

The article published in this issue by Dr. Llewellys Barker on therapeutic measures; the papers read at the last meeting of the American Medical Association in the section devoted to Pharmacology and Therapeutics by Rountree, Young, Crile and others; the last presidential address of the British Pharmaceutical Association; the address of the President of the American Medical Association calling attention to a renewed interest in pharmacy and therapeutics; the examples of the close union of schools of pharmacy with hospitals in Germany and the efforts being made in this direction in this and other countries, are but evidences that a new era is at hand in the history of pharmacy and that its growth in usefulness and importance in the interests of humanity and medicine is so well advanced and determined that we can not afford to fail to respond to the inspiration of the great work planned by all thinking minds for the decade to follow.

The Philadelphia College of Pharmacy and Science, for the past one hundred years has been a leader in all that pertains to pharmacy and the allied sciences and the progressive element in the Board of Trustees, the Faculty and the College body appreciate fully the importance of the present movement and desire that this institution shall be among the foremost to join in the efforts to advance the interests of this great profession with all its varied interests and ramifications in both the professional and business world.

With this end in view, the efficiency of the College has been improved and enlarged, made possible by the financial assistance of the Board of Trustees and a few friends of the institution. The College has been renovated and repaired to try to provide proper,

adequate and comfortable quarters for its work and its faculty and curriculum expanded to meet the demands of the awakening interest in pharmacy and therapeutics. The allied branches of the work—general chemistry, industrial chemistry, physiological chemistry, bacteriology—have equally been provided for and at the same time measures have been taken to raise the general standard of educational pre-college work, which has already brought to the institution a class better equipped for the work than ever before. To supply a broad and thorough basic education as a preparation for our professional courses, instruction in the languages, in mathematics, and in business methods, has been provided, in order that the graduate shall go forth well equipped for work in the world and with a foundation that makes possible successful life work whether it be in pure pharmacy or its business branches, such as the retail drug business or the great manufacturing houses or in the work of pure research whether it be botany or chemistry or physiology or bacteriology. It will be the effort of the College to provide instruction in its regular and post-graduate work which will enable its students to successfully enter the fields of life work in the many splendid openings existing today as real pharmacists, as analytic chemists, as directors of great sanitation problems, as research workers either independently or in the great laboratories of our educational and industrial institutions, to be directors and assistants in the bacteriological and biological laboratories of educational institutions, of general and municipal governments, in the great drug manufacturing laboratories, to carry on work of this kind in pharmacies and drug stores which maintain laboratories great or small and to be the skilled assistants of physicians in those important branches of their practice involving all that pertains to the chemical, bacteriological, biological examinations of their patients and which the physician has not the time and often not the technical skill to perform.

A glance shows the vast importance, the numerous splendid openings for the work contemplated by the present organization of the College. It must not be overlooked also that the pre-professional work to be obtained in this College provides the best possible basis for those who intend ultimately to study and practice medicine. In fact it must be apparent that no medical man can hope to enter on his profession, equipped for research and scientific medical attainment without the basal information given in the work of this school.

The fact that medicine and pharmacy have grown apart during

the past years is regretted by both professions and their closer union is absolutely necessary for the success of each in its humanitarian work.

The great need of the present day as Dr. Rountree states at the close of his address before the Section on Pharmacology and Therapeutics of the American Medical Association is the establishment of a "National Institute of Pharmacology and Experimental Therapeutics."

This idea has been in the minds of some of the trustees and officers of the College and it has been thought that a movement along this line might be contemplated with the College of Pharmacy and Science of Philadelphia as a center, linking up its work with a great hospital existing or to be built in the city in connection with a manufacturing plant under the control and direction of the College, with an adequate animal farm for biological products and an extensive botanical and research garden for the systematic study, cultivation and standardization of therapeutic drug plants.

This would allow the equal and co-ordinate union of the College for teaching, research and standardizing all that pertains to pharmacy and its allied branches in chemistry and bacteriology, the proper preparation for safe and scientific administration of its products and the determination of their value at the bedside in the associated hospital by the best staff of attending and consulting physicians the city could produce. This would bring about, ideally, the union of the doctor, the scientific pharmacist and the highest and best method of making the therapeutic agent for human use. As a co-ordinate body they would work constantly together and the final approved therapeutic agent, with its full history, characteristics, mode of application and method of manufacture would then be given to the world for its use and to the commercial manufacturers for production. No commercial element enters into this proposed organization. For this purpose a sufficient endowment must be raised to place the College, the hospital, the manufacturing plant absolutely outside of any possible commercial implication. If possible the patients at the hospital should be free patients, but given the best of every hospital attention and equipment. Philadelphia, which needs so acutely, larger facilities for the care of its sick, could well assist to make so magnificent a contribution to the welfare of its population and indirectly to that of the world.

This outline of the visions of the possibilities of the future it is

hoped will stimulate thought and action in the forward movement of the work and help lead to the assistance and solution of the great problem before us.

The College possesses already on its staff men of splendid attainment and untiring energy and courage to prosecute its work. Never have I seen a group of educators better equipped to inspire the young, to give instruction that has real, practical, useable worth in the life work. With the increase in the faculty more time will be given for problems of research, which in the past has been so important, inspiring and valuable. It is hoped when the reorganization is complete that the resources of the College may be made available to the outside world in order that its problems may be referred to our research workers for solution and if this work can be provided practically free of charge, many a splendid idea may result in practical fulfillment and use.

In view of the splendid possibilities can there be one among us who will not do his utmost to see that at last pharmacy may be given its fair chance to develop itself in the world's work?

W. C. B.

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## SELECTED EDITORIAL

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### THE LIVE WIRE MIND.

When a mentality like Edison's sets questions, such as have been widely discussed and criticized, it behooves more commonplace minds to "stop, look and listen." Mr. Edison, quite unintentionally, has stirred the educational world and, as in all such stimulations of the gray matter, we find ourselves getting "back to the Greeks," the source of all philosophical thinking and initiative. The mind of an inventor is an inquiring one: he is not content to tread the old beaten paths around, but tackles, directly, the obstacles in front. To do this, observation of all sorts and conditions of things keeps the mind supple and alert. Some of these queer shaped and unimportant bits of knowledge may be found to fit into these other equally odd shapes and, little by little, his picture puzzle reveals a perfect whole. Who would have supposed that the study of the anatomy of the mosquito would reveal the true source of malarial fever, and that by this knowledge vast areas of the earth would be reclaimed for

habitation? When Joseph Leidy noticed and questioned what might be the white specks in the ham served for his luncheon, his mind opened the way to the discovery of the parasite disease in pork, against the eating of which, as told in the Book of Leviticus, the Jews had blindly enacted laws centuries before. The large majority of us are of the cog and ball-bearing type of mind. Specialization today is begun so early that the foundations of knowledge and philosophical thinking are very narrow. The question of moment to American educators is whether our schools and colleges are developing the greatest number of observers possible, or whether the ordinary student is constrained to tread the beaten paths with never a look to right or left and never an impulse to inquire into the mysteries that lie near by. The man of the bush who first used ash or hickory for his axe handle was a greater observer than the college man who thought cork came from Ireland. A man with an inquiring mind is what Edison calls a "live wire," interesting and interested; and in no way does this interfere with his being a highly specialized technical expert in any line he may be engaged in. Is our system of education making for or against this mind development? It is not whether a man can answer correctly all these questions, but whether he is asking these and similar questions of himself when he meets them in his daily reading and conversation. It was mind exercise and not mere knowledge that enabled the Greeks to initiate, in physics, geometry, literature, art and on through a long list, the foundations on which we build today. So, "back to the Greeks," who taught us observation, general and specific, with philosophical deductions. Concentration has its advantages; but unless the object is held at sufficient distance, the observer looks cross-eyed and loses his sense of proportion.—(*Jour. of the A. M. A.*, Aug., 1921.)

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## ORIGINAL PAPERS

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### THE CHEMICAL ELEMENTS OF LIVING MATTER.

By INGO W. D. HACKH,

COLLEGE OF PHYSICIANS AND SURGEONS, SAN FRANCISCO.

It is a remarkable fact that relatively small number of elements enter into the composition of living matter, whether of vegetable or animal nature. Naturally the elements, excepting oxygen, enter the

metabolism of the cell organism, not as free elements, but as compounds. These compounds we speak properly of as *food*, of which there are the four great classes of proteins, carbohydrates, fats, and salts. The first three classes all contain hydrogen, carbon, oxygen, and sometimes nitrogen. These four elements are of paramount importance in all life processes, and the multitude of compounds, which they are able to form, is the main study of biochemistry. To indicate the service of these elements in the living organism is the aim of this article, although present knowledge is far from complete. The importance of the elements is shown in the three groups:

- a. The true life elements or bioelements which are invariably present in all vegetable or animal matter;
- b. Elements which commonly occur in cell organism, and which seem to be characteristic of certain tissues;
- c. Elements occurring rarely in the living organisms, which seem to be more or less adventitious.

#### THE TRUE LIFE ELEMENTS OF BIOELEMENTS.

1. *Carbon*, well known as the structural element which gives to the large number of organic compounds their complexity of form and function, is the corner-stone of organic cell metabolism. Its valency of four is significant, as it explains the fact that an atom of carbon has to another carbon atom a greater affinity than to an atom of another element. In other words the attractive power of a carbon atom is greatest<sup>1</sup> to another carbon atom for its electromotive force is nearly zero, it can act therefore sometimes as positive, sometimes as negative atom and produces the many chains and rings of organic compounds. According to the latest theories of chemistry, the stable compounds all contain eight or a multiple of eight valence electrons, these alone forming a stable system.<sup>2</sup> Carbon, having four valence electrons, combines therefore readily with other carbon atoms to an octet or stable system of eight electrons.<sup>3</sup> The recognition of this ability of the carbon atom will explain its pre-

<sup>1</sup> Geoffrey Martin, Ueber das Affinitaetsgesetz im Per. Syst., Inaug. Diss., Kiel, 1906; page 23.

<sup>2</sup> Lewis's theory of cubical atom, Parson's theory of magneton, Langmuir's octet theory and others.

<sup>3</sup> *E. g.*, sodium has 1 free valence electron, chlorine has 7, thus NaCl has together 8 valence electrons. Hydrogen has 1, in CH<sub>4</sub> there are thus 8, in C<sub>2</sub>H<sub>6</sub> 16 or (2x8) valence electrons.



dominant function as the substance endowing complexity, variability and individuality to organic compounds.

2. *Hydrogen*, constituent of water and present in all acids and bases, plays an important role in biochemical reactions. Free hydrogen gas, a mild reducing agent, is formed as fermentation product and occurs in the intestinal gases of mammals, the result of bacterial composition of the carbohydrates:

*Composition of Intestinal Gases (Ruge)*

100 volumes contain	H <sub>2</sub>	N <sub>2</sub>	CO <sub>2</sub>	CH <sub>4</sub>
in vegetable diet	1-4	10-19	21-34	44-55
in meat diet	1-3	45-64	8-13	26-37
in milk diet	43-54	36-38	9-16	1-2

Many biochemical reactions are due to the formation of water or neutralization  $H + OH = H_2O$ . Free acids or  $H^+$  (hydrogen ions) are of importance in gastric digestion and animal respiration. Bases or hydroxyl ions ( $OH^-$ ) occur in the saliva and other secretions. The splitting off of water takes the place in the synthesis of carbohydrates while the taking up of water occurs in the hydrolysis or breaking down of the carbohydrates. To the great affinity of hydrogen for oxygen, many other reactions must be ascribed which involve the dissociation and separation of oxygen from various compounds. Hydrogen, therefore, is the active principle in the cell metabolism which is readily oxidized, and performs the service of a reducing agent.

3. *Oxygen*, the great oxidizer, circulates in the cell-organism as the releaser of energy,—it is the energy carrier of life furnishing heat and power to the living machines. Both hydrogen and oxygen are, as water, the principal constituent of protoplasm,—without water there could be no cell-life. But free oxygen is the great sustainer of life, it is absorbed by the blood of animals, and carried to every cell in need of it, yielding by its reactivity heat and energy.

*Composition of the Gases of Blood*

100 vol. blood contain	O <sub>2</sub>	N <sub>2</sub>	CO <sub>2</sub>
of arterial blood	18	2	40
of venous blood	12	2	48

Oxygen is not only the most abundant, but also the most important element and its discovery laid the foundation of modern chemistry.

To the cell metabolism oxygen is the element which burns up the waste-products and oxidizes food materials thereby liberating the stored energy in the form of heat.

4. *Nitrogen*, the apparent inert and lazy gas of the atmosphere, is the element giving instability and therefore reactivity to organic compounds. Nitrogen can form several series of compounds which are more or less readily transformed into each other. Thus there are the compounds of the lowest valence number ( $-3$ ) or compounds derived from ammonium ( $\text{NH}_3$ ), to this class belong the amino acids ( $\text{NH}_2\text{-R-COOH}$ ) which are the bricks or building stones of the proteins. The next series of compounds are derived from nitrous oxide ( $\text{N}_2\text{O}_3$ ) with a valence number of  $+3$  and in this series there are the nitrites, which are readily oxidized to nitrates. Finally the compounds derived from nitric oxide ( $\text{N}_2\text{O}_5$ ) form the nitrates (valence number  $+5$ ) and are the highest stage of oxidation. Nitrates are important as fertilizers from which the plant synthesises the complex proteins by reducing processes. Nitrogen forms with C, H, and O a number of important radicals and compounds, its rôle in the cell-metabolism seems to be the imparting of instability and sensitiveness to protoplasmic compounds.

5. *Phosphorus*, the controlling element, is indispensable to the nucleus of the cell. It occurs in nucleins, lecithins, and vitellins; is essential for nerve and brain cells of animals, and accumulates in seeds and buds of plants. It is a constituent of chromatin, the intranuclear germ plasm, which is supposed to be the seat of heredity.\* It is essential in the assimilation of fats which are transformed into lecithins before assimilation and seems to accumulate in those parts of the cell-organism where the important function of cell-division is performed:

*Content of  $\text{P}_2\text{O}_5$  in the Ash of Plants:*

*.100 parts of plant ash contain  $\text{P}_2\text{O}_5$*

in roots average	12-17%
in stems "	4-12%
in leaves "	9-13%
in seeds "	37-49%

\*Osborn, Origin and Evolution of Life; N. Y., 1917; page 21 ff.

In ionized form, as phosphates of sodium and potassium, it maintains the neutral reaction of blood and other liquid tissues (buffer solution). The solid phosphates of calcium and magnesium are predominant in the skeletons of animals. Small doses of phosphorus stimulate the brain and circulation, the function of the genital organs, and the growth of bones. Phosphorus is thus the regulating and controlling element of the cell metabolism.

6. *Sulfur*, as essential constituent of the proteins, is invariably present in animal and vegetable organisms. It is a constituent of the aminoacid cystin and so occurs in keratin or the epidermal protein, in connective tissues, in taurocholic acid of the bile, and as sulfates in blood and other liquors. Free sulfur occurs in the protoplasm of certain protozoa or unicellular animals. Hydrogen sulfide is a constituent of the intestinal gases of vertebrates, formed together with mercaptans from the decomposition of proteins rich in cystin. Sulfocyanates occur in saliva, nose secretions, and urine, while sulfuric acid has been found in the saliva of certain snails as the product of bacterial metabolism. The ash of plants contains on an average from 0.7—7% of  $\text{SO}_3$ .

7. *Magnesium*, present throughout the cell organism, occurs especially as magnesium phosphate in bones, teeth, blood, muscles and nerves of the vertebrates. It is abundant in many lower animals (*e. g.*, corallinaceae). As permanent constituent of chlorophyll it is essential to the metabolism of plants. Aetiophyllin  $\text{C}_{31}\text{H}_{34}\text{N}_4\text{Mg}$ , a constituent of chlorophyll, is a substance closely related to hæmophyllin of the hæmoglobin of blood. Magnesium has a close relation to phosphorus, for it is more abundant in the plant parts undergoing development (seeds and growing tips) and is absent in maturing organs. Oily seeds contain more Mg than starchy seeds,—by the absence of Mg no oil is formed. It is a vehicle for the assimilation of phosphoric acid and so aids indirectly the formation of nucleoproteins.

*Content of MgO in the Ash of Plants:*

*100 parts of plant ash contain MgO*

in roots, average	3.7%
in stems, average	2.4%
in leaves, average	4.12%
in seeds, average	8.17%

8. *Iron*, the respiratory metal of animals, is present in all protoplasm and is essential to the formation of coloring matter (chlorophyll of plants, hæmoglobin of animals). In hæmoglobin it serves higher animals as an oxygen carrier (1 gm. Fe to 150 gm. of red blood corpuscles). The human body contains about .005% iron, it occurs in bile, lymph, chyle, gastric juice, pigment of eye, milk and in urine. Its most important function is its presence in hæmatin  $C_{34}H_{84}N_1FeO_5$  of the hæmoglobin which acts as transmitter of oxygen from the lungs to the tissues, and of carbon dioxide from the tissues to the lung (respiration). It is also invariably present in the vegetable organism:

*Content of  $Fe_2O_3$  in the Ash of Plants:*

<i>100 parts of ash contain</i>	<i><math>Fe_2O_3</math></i>
in roots, average	0.8-2%
in stems, average	0.6-4%
in leaves, average	0.5-1%
in seeds, average	0.5-2%

Lack of iron leads to pathological chlorosis; in plants the leaves do not seem able to form chlorophyll, become pale and unable to photosynthesis.

9. *Potassium*, the most electropositive metal, is essential to the living tissues of plants and animals. It occurs in two forms: (a) ionized as chlorides, phosphates, sulphates and carbonates, and (b) masked in organic combination as constituent of a large molecule. In the regulation of life processes the potassium salts play an important rôle as stimulating agents, acting on the brain, vasomotoric and sensory nerves of animals. In the plant organism it is important in the formation of carbohydrates and proteins, for without K no starch is formed. Seeds and other organs rich in proteins are usually rich in potassium:

*Comparison of Protein and Potassium:*

<i>100 parts contain</i>	<i>Protein substance. of dried</i>	<i>of ash.. Potassium</i>
Seeds of cereals, average	10.2%	23.07%
Seeds of legumes, average	29.0%	39.2%

*Content of  $K_2O$  in the Ash of Plants:*

<i>100 parts of ash contain</i>	<i><math>K_2O</math></i>
in roots, average	45.60%
in stems, average	13.47%
in seeds, average	23.42%
in leaves, average	26.36%

Certain fresh water and marine plants are able to store large quantities of potash, *e. g.*, the Pacific Coast Kelps (*Phæophyceae*). A small percentage can be substituted by the other alkali metals. Potassium occurs mainly in the cell-membranes and tissues and seems to act as osmotic agent. The saps and juices sometimes contain K which may be replaced by sodium.

ELEMENTS WHICH COMMONLY OCCUR IN CELL ORGANISM.

10. *Fluorine* is found in small amounts in bones (0.05-0.2% of ash), teeth (0.18% of ash), brain matter (0.8 mg. in 100 gm.), cow's milk (0.3 mg. in 1 liter), egg-yolk (1.1 mg. in 100 gm.). It occurs also in blood where it seems to play a protective and regulative part in the process of coagulation of fibrin. It is also found in certain mollusks and many plants.

11. *Chlorine* because of its abundance in sea-water is present in marine algæ and many other plants, though it seems to be not essential for the complete development of higher plants. It is essential to animals, occurring mainly as NaCl in blood, lymph, tears, sweat, and urine. As free HCl of the gastric juice, it takes part in the digestion of food. The percentage of Chlorine in different tissues is

blood	0.268% spleen	0.107% bonemarrow	0.034%
lungs	0.150% brain	.100% muscles	.033%
skin	0.145% stomach	.093% liver	.025%
kidney	.122% intestine	.040% bile	.010%

12. *Bromine* occurs in traces in all organs of mammals. It is abundant in marine algæ, but little is known of its function.

13. *Iodine* is essential to vertebrates as a constituent of iodothyryn of the thyroid gland. The amount of I in the gland is variable from 0.077-3.85 mg. of iodine per 1 gm. of the dry substance

of the gland (fresh weight of gland in adults 29 to 231 gm., dry substance from 5 to 62 gm.) Iodine occurs in star fishes from 0.007-0.24%, in sponges 1.5% (as iodospongin  $C_{56}H_{87}IN_{10}S_2O_2$ ), in oysters, sea weed, and especially brown algæ, while the corals, *Gorgonia Carolinii*, may contain from 0.7-7.8% of I. Besides in the thyroid gland iodine is reported in the following organs and tissues of man:

liver 1.214 mg. I in 100 gm.	skin and hairs	0.88 mg. I
kidney 1.053	blood, menstrual	0.09 "
stomach .909	" normal	0.021 "

14. *Silicon* is always present in small amounts in vertebrates, mainly as a constituent of the teeth and bones:

*1000 grams of dry substance contain*

enamel of teeth	0.581 gm. $SiO_2$ , tendons	0.064
Wharton's jelly	0.243 " " skin	0.044
dura mater	0.087 " " muscles	0.024

It is also present in radiolarians and siliceous sponges and is found in all plants, predominant in the stems of many grasses, in diatoms and in marine algæ. Cereal straws and corn stover may contain 40-70%,  $SiO_2$  equisetaceæ 70-80%  $SiO_2$  of their ash. It appears to be chiefly in the cell wall and to act as support and protective substance.

*Content of  $SiO_2$  in the Ash of Plants:*

*100 parts of ash contain  $SiO_2$*

in root, average	1-3%
in stems, average	6-70%
in leaves, average	5-40%
in seeds, average	0.5-3%

15. *Sodium* is essential for animals but not plants. It is abundant in blood and lymph and also occurs in many plant saps and juices. In muscles (5-6%), brain (1½-2%), and liver (2%) there is more K than Na, while the proportion of K:Na is equal in heart and kidney, but in the pancreas (1-4-1-3%), spleen (5%), and bones (6%) there is more Na than K; and cartilage contains only sodium. Like K it has an osmotic function.

*Content of Na<sub>2</sub>O in the Ash of Plants:*

*100 parts of ash contain Na<sub>2</sub>O*

in roots, average	2-10%
in stems, average	1-4%
in leaves, average	0.8-2%
in seeds, average	0.6-2%

16. *Calcium* is widely distributed in animals and plants and is important in regulating biochemical reactions through irritability and stimulation; *e. g.*, in vertebrates the clotting of blood, in plants the protein formation of calcium proteids, nucleo-proteins, and plastides of cell. In vertebrates the skeletal material is chiefly calcium phosphate, in invertebrates calcium carbonate. There are in

muscles	.005% CaO	pancreas	0.15% CaO
blood	.006%	lungs	.016%
brain	.009%	liver	.029%
kidney	.009%	heart	.025%

In the plant organism it accumulates in leaves and vegetative organs and there appears to be a relation between the Ca content and carbohydrate digestion.

*Content of CaO in the Ash of Plants:*

*100 parts of ash contain CaO*

in roots	2-11%
in stems	5-25%
in leaves	6-32%
in seeds	2-9%

17. *Manganese* always appears in traces in animals and plants. It is found not only in blood (0.5-2.5 mg. per liter), milk bones, hairs, tissues of mammals, but also in the ash of plants. Manganese salts have recently been considered as fertilizer for plants,<sup>5</sup> but their rôle in the metabolism is little understood. They seem to act as stimulants and irritants by regulating the motor activities of the cell organism. The large amount of Mn in the ash of the pancreas (2.2-2.5%) is remarkable.

18. *Aluminum* is abundant in soil and therefore widely distributed in plants. Cryptogams contain Al mainly in their stems, while angiosperms have much Al in their blossoms and flowers. Pine needles are especially rich in aluminum.

\* U. S. Dept. Agricult., Bull. 600, 1917.

## ELEMENTS OCCURRING RARELY IN LIVING ORGANISMS.

19. *Lithium* occurs, in traces, apparently in all animals and plants and seems to be a constant constituent resembling the other alkali metals in its function. The lungs of mammals contain lithium salts. Lithium compounds are rapidly absorbed and eliminated by the kidneys—no case of poisoning has so far been recorded.

20. *Rubidium* is found in various animals and plants.

21. *Cesium* occurs in traces in some animal organs and in many plants (timothy, raspberry, beets, etc.).

22. *Strontium* is present in animals and plants in variable amounts and seems to be of accidental occurrence.

23. *Barium* is found in some plants grown on soil containing barytes.

24. *Radium* occurs in minute traces in animals and plants.

25. *Boron* is sometimes found in the ashes of plants, especially if grown on soil rich in tourmalin and its decomposition products (Belgium, So. California).

26. *Zinc* has been reported in the human liver (10-76 mg. per kg.); traces are also found in corals and some plants.

27. *Copper*, while not essential for vertebrates, occurs in the human body; especially in the blood, brain, kidney (1.2-2 mg. per kg.), spleen (3.2-5.6 mg. per kg.), liver (1.5-15 mg. per kg.). It is essential for invertebrates where it plays the same rôle which iron does in vertebrates, namely as respiratory metal and oxygen carrier in the form of hæmocyamin. The bluish blood of molluscs (Cephalopoda and Gastropoda) contain large amounts of copper (*e. g.*, oysters, octopus, lobsters, helix pomatia, Limulus cycleps and Sabella species). It has also been found in the plumage of a bird, the turaco or Cape Lory, whose red feathers contain turacin (7% Co.).

28. *Nickel* and 29. *Cobalt* occur in traces in some plants.

30. *Chromium* is occasionally found in small amounts in some plants.

31. *Vanadium* is exceedingly rare, found only in few cases.

32. *Titanium* is found in slight traces in nearly all plants and appears to be a constant constituent like silicon.



33. *Cerium* occurs in traces in some plants. As oxalate it has been found in bones (0.03 gm. Cerium oxalate in 1 kg).

34. *Tin* and 35. *Lead* have been found in some organs. Human kidney, liver, hairs, and nails contain traces of lead; some corals contain small amounts of lead.

36. *Arsenic* occurs in some animals and many human organs. In chronic arsenic poisoning the amount of As in the skin is increased considerably, often causing a brown pigmentation of the skin, probably due to the formation of sulfides. (Keratin contains S.) The minute traces of arsenic in human organs are:

skin	.0026 mg.	As in 100 gm.	liver	.0019 mg.	As in 100 gm.
pancreas	.0029 mg.		kidney	.0015 mg.	
hairs	.0049 mg.		brain	.0013 mg.	

Elements found in isolated cases in animals and plants are: Geranium, thallium, mercury, solenium, silver.

No other elements have been reported to enter into cell organism.

Summarizing the occurrence of elements in living organisms, vegetable or animal, only four elements form its bulk, namely 97-99% of which O = 52-63%, C = 20-38%, H = 7-10% and N = 0.03-3%. The lowest plants have in addition S, K, and Ca,—while the chlorophyll-containing plants also contain P, Mg, and Fe,—in animals Cl, Na, Si, and I are necessary. It appears that with complexity of functions the number of elements taking part in cell metabolism increases; hence the more highly developed an organism, the greater the number of elements which enter into its composition and which are thus usually present in some highly specialized organ; as *e. g.*, iodine in the thyroid glands.

Considering the living organism as a chemical machine consisting of protoplasmic units or cells, it appears that the essential elements function in two ways: (a) As component parts of the cell structure; *e. g.*, S in the cell wall and the epithelial tissue, P in the nucleus, Si in the stem of certain plants, Ca in the skeleton of animals and the stems of plants; and (b) as agents causing physical or chemical reactions; *e. g.*, the respiratory metals Fe (vertebrate blood), Mn, Cu (invertebrate blood), K in the root of plants, Mg in seeds and leaves.

Many of these elements are associated and occur in pairs, thus in the vegetable metabolism Mg and K are predominant, while the corresponding pair in the animal organism is Fe and Na. These two pairs are also found in igneous rocks.<sup>6</sup> Again there is an accumulation of certain elements in definite tissues of the organism, thus in the vegetable organism the seeds are rich in P and Mg and depleted of Ca and K, while the stems and leaves contain much Ca, K, and often Si, and the roots are rich in K and depleted of P.

The specific rôle of the elements is little understood and so it is speculative to account for their presence. It seems that the presence of an element, other than the 9 or 12 essential ones, is the result of either evolution or adaptation. Thus the occurrence of iodine in the thyroid gland of vertebrates seems the result of evolution; *e. g.*, the utilization in a highly specialized organ of the organism, while its presence in marine plants and invertebrates seems the result of adaptation, *e. g.*, diffused throughout the cell organism with apparently no distinct function. Likewise the presence of copper in the blood of certain invertebrates seems due to evolution, while its presence in bacteria, grown successively for several generations upon a copper containing culture media, is adaptation.

An interesting comparison of the distribution of elements in living organisms and inanimate nature with its relation to the periodic system has been pointed out in previous papers<sup>7</sup> where it was shown that the elements of low atomic weights essential and occurring in living matter, cluster together in the periodic table and seem to point to an evolution. There are many unsolved questions in this fascinating problem. Why did the cell substitute in specialized tissues the elements of higher atomic weight for those of lower atomic weight, *e. g.*, Br and I for Cl and F? Is the answer merely to be found in physico-chemical phenomena, or has that mysterious controlling force guarding the entrance to the protoplasm exerted a selective process for a certain end? Is this force, the vital force, possessed of intelligence and not of a purely physical or chemical nature?

<sup>6</sup> H. S. Washington, *Sci. Am. Suppl.*, Vol. 83, page 27, 1917.

<sup>7</sup> *Journal of General Physiology*, Vol. 1, page 429, 1919, and *Science Progress*, Vol. 14, page 602, 1920.

## CONCERNING THE THERAPEUTIC ACTION OF SOME DERIVATIVES OF COD LIVER OIL.\*

By OSCAR BERGHAUSEN, B. A., M. D., and LOUIS A. STEINKOENIG,  
Ch. E., Cincinnati, Ohio.

### HISTORICAL.

The fatty oils have had a wide therapeutic application especially in the treatment of leprosy. Chaulmoogra oil derived from the seeds of *Taraktogenos kurzii*, was used for many years at the Molokai Settlement, and previous to 1865 by physicians in India in the treatment of leprosy. An excellent historical review of the chaulmoogra oil treatment of leprosy was published by George W. McCoy.<sup>1</sup> Power and his collaborators<sup>2</sup> discovered a new series of fatty acids represented by two members—chaulmoogric acid,  $C_{18}H_{32}O_2$ , and hydnocarpic acid,  $C_{16}H_{24}O_2$ , which they prepared from chaulmoogra oil.

The report of Dr. Victor G. Heiser<sup>3</sup> caused renewed interest in this mode of therapy and seemed to show that there were one or more active principles which had a specific action in leprosy and that this agent was more effective when given hypodermically or intramuscularly than when taken by mouth. Sir Leonard Rogers used the sodium salts of acids derived from chaulmoogra oil, using the fractions separated by Ghosh.<sup>4</sup>

In a more recent publication Sir Leonard Rogers<sup>5</sup> describes the use of gynocardate of soda and morrhuate of soda, the latter referring to the sodium soap of the fatty acids prepared from cod liver oil. Rogers suggests that "other unsaturated fatty acids may also be expected to yield effective preparations against the acid-fast bacilli of both leprosy and tuberculosis." McDonald and Dean<sup>6</sup> later published results using distilled esters of the fatty acids of chaulmoogra oil.

### SODIUM MORRHUATE.

Becoming interested in this subject we determined to study the therapeutic value of sodium morrhuate and the hitherto undescribed mercury salts of morrhucic acid. A. Gautier and L. Mourgues<sup>7</sup> ex-

\*Read before the Daniel Drake Society, Cincinnati, Ohio, June, 1921.

tracted cod liver with acidified alcohol and refined the extract, isolating finally a yellow oil which crystallized in the form of plates. They called this substance morrhuic acid  $C_9H_{13}NO_3$ , assigning to it the structural formula of hydroxidihydropyridine-butyric acid.

Sodium morrhuate can readily be used in the form of a 3 per cent. aqueous solution as suggested by Sir Leonard Rogers. If a sediment forms the supernatant solution can be used. This keeps at room temperature if 0.25-0.50 per cent. carbolic acid is added. It has a reddish brown color and a distinct odor of cod liver oil, and represents the sodium salts of mixed, unsaturated fatty acids.

Deep muscular injections of from one to four cubic centimeters have been given. The patient complains of some local tenderness lasting for a day or two, but these reactions are never severe. Intravenous injections are well tolerated, larger amounts causing a slight headache and a feeling of dullness, but general reactions in the form of chills and fever have not occurred. We have not noticed any evidences of phlebitis in the vessels selected for injections. It has been suggested that sodium morrhuate given intravenously could possibly lead to a stimulation of the immunologic mechanism concerned in the healing of infectious processes non-tubercular in nature. A limited experience in this field has failed to verify these predictions. We have not as yet tried out this new remedy in a series of patients suffering from pulmonary tuberculosis.

#### CALCIUM MORRHUATE.

By adding calcium acetate to a solution of sodium morrhuate containing  $1\frac{1}{2}$  per cent. gelatin and  $\frac{1}{4}$  per cent. carbolic acid, a suspension of calcium morrhuate was obtained. One c. c. of this suspension contained  $\frac{1}{6}$  grain of calcium morrhuate and  $\frac{1}{70}$  grain of gelatin;  $\frac{1}{2}$  per cent. aqueous formaldehyde solution can be used as a preservative. When these insoluble suspensions were given intramuscularly some local tenderness developed but no general symptoms.

#### MERCUROUS MORRHUATE.

The mercurous preparation was found to be greyish in color, homogeneous, gelatinous and sticky in nature, and suitable for intramuscular medication in patients suffering from syphilis. It

was prepared by adding a newly made aqueous solution of mercurous nitrate to a 3 per cent. solution of sodium morrhuate to complete precipitation, washing and drying the precipitate in a current of warm air. Collapsules\* containing 3 grains of mercurous morrhuate, representing 50 per cent., *i. e.*,  $1\frac{1}{2}$  grains of metallic mercury were made at our request, by two prominent capsulating houses. Many of these collapsule injections were made and have been found to be very satisfactory. The contents can readily be expressed from the collapsules without preliminary warning. (The amount of local reaction produced about equals that obtained with the ordinary two grain "salicidol" preparations.) Patients have not complained of the severe local reactions so common with the ordinary preparations heretofore employed.

#### MERCURIC MORRHUATE.

Mercuric morrhuate was obtained by adding a warm dilute solution of mercuric chloride to a warm dilute solution of an equivalent amount of sodium morrhuate, slowly and with thorough agitation. A reddish yellow, opalescent colloidal solution resulted. When an attempt was made to remove the sodium chloride and uncombined mercuric chloride by dialysis, the colloidal solution of mercuric morrhuate agglomerated. For this reason a more suitable preparation for intravenous medication was obtained by carefully calculating the amount of mercuric chloride required and making the suspension neutral to phenolphthalein by using a small quantity of dilute potassium hydroxide. This kept perfectly at room temperature only a slight precipitation taking place on standing.

It was found that syphilitic patients could tolerate as much as 3 c. c. of this suspension intravenously, without producing general manifestations. In one young girl of eighteen years, suffering from congenital syphilis, temporary symptoms vascular in origin developed after giving about 2 c. c. intravenously. When this preparation was added drop by drop to ordinary clear human serum, no precipitation of protein occurred. When added to freshly drawn blood in

\*Mr. L. W. Cyrenius, of the American Collapsule Company and Dr. Sheridan Baketel, of the H. A. Metz Company, were kind enough to prepare these collapsules, using the same medium as employed in the preparation of "salicidol."

the proportion of 0.5 c. c. to 2 c. c. of human blood and allowed to stand for ten minutes, no clumping occurred, and when centrifuged the supernatant plasma showed the merest trace of hemolysis. These results would indicate that the mercuric suspension is probably safe for intravenous medication.

#### LITERATURE.

<sup>1</sup> Studies upon Leprosy, xxviii, per *Public Health Bulletin* No. 175, January, 1916, pages 3-11, Government Printing Office, by Geo. W. McCoy and Harry T. Hollmann.

<sup>2</sup> Power and Gornall, the Constituents of Chaulmoogra Seeds. *Journ. Chem. Soc.*, lxxxv, page 838, 1904.

<sup>3</sup> *Public Health Reports*, Vol. 29, No. 22, page 2763.

<sup>4</sup> Sudhamoy Ghosh, Report of a Chemical Investigation of Chaulmoogra Oil in Connection with Leprosy Treatments. *Indian Journal Medical Research*, IV, page 691 (1916).

<sup>5</sup> Paper read before the Medical Section of the Asiatic Society of Bengal, March 12, 1919, by Sir Leonard Rogers.

<sup>6</sup> The Treatment of Leprosy. Reprint No. 607, from *The Public Health Reports*, August 20, 1920, pages 1959-1974.

<sup>7</sup> *Compt. Rend.*, 1888, 107, 740.

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## ABSTRACTED AND REPRINTED ARTICLES

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### THE VALUE OF DRUGS IN INTERNAL MEDICINE.\*

By LEWELLYS F. BARKER, M. D., Baltimore.

We are now witnessing a cautious revival of the use of drugs in the treatment of disease. During the last half of the nineteenth century pharmacotherapy fell more or less into discredit, owing (1) to a reaction against the scandalous abuse of the "shotgun prescription," (2) to the general therapeutic nihilism that followed the rise of studies in pathologic anatomy, and (3) to the growing recognition of the importance of forms of therapy other than treatment by drugs. Though in some quarters the denial of pharmacotherapy was pushed to extremes, it is now generally admitted that the move-

\*Read before the Section on Pharmacology and Therapeutics at the Seventy-Second Annual Session of the American Medical Association, Boston, June 21, 1921. Reprinted from *Jour. Amer. Med. Assoc.*, October 8, 1921.

ment against the indiscriminate and noncritical use of drugs, to the relative exclusion of other and often more efficacious methods of therapeutic intervention, was necessary and timely, in order that the more rational therapy of our period might emerge.

In the therapy of today, based on more accurate diagnosis and on enlarged conceptions of pathologic physiology, etiology and pathogenesis, a new hopefulness prevails. We make use now of a host of methods that are found to be trustworthy for healing, for palliating and for preventing. Along with diet, baths, climate, air, light, heat, exercise, massage, electricity, roentgen rays, radium, serums, vaccines, mechanical appliances, surgery, nursing, and psychic and social influences, drugs are gradually finding their proper place in the therapeutic armamentarium of the medical practitioner. For among the drugs of various sorts, including both natural substances and pure chemicals provided by separation or by synthesis, there are agents that can now be employed with great confidence and often with the happiest results.

#### DUTY OF THE INTERNIST.

In the management of patients and in the treatment of their diseases, it is our duty as physicians to see to it that we do not neglect to make application of any of the agents at our disposal that may reasonably be expected to help. Briefly to survey the help offered to the physician in his daily work by modern pharmacotherapy is the object of the present symposium. The time allotted will, of course, not permit of any detailed discussion of the use of single drugs. It is, I take it, the intention of those who planned the symposium that it should deal rather with the general principles that underlie the use of drugs in therapy, and with certain examples of the application of these principles in practice. Others are to speak of the use of drugs by surgeons and by specialists; this paper has to do with their use by the internist.

Man desiring to help his suffering fellow man must not lack—indeed, has never lacked—courage. Think, for example, of the boldness of the surgeon who annihilates the consciousness of his patient and then, without trepidation, cuts into the abdomen, or excises a goiter, or removes a brain tumor! The physician also must have bravery, one might almost say audacity, when he attempts, by the use of a drug, to intervene favorable in the disturbed physical, chemical and biologic processes of the human body in disease.

## COMPLEXITY OF CHEMICAL PROCESSES.

Man's body is the most marvelous chemical laboratory in the world, a laboratory made up of several thousand billions of separate work rooms, in each of which the amount and kinds of work done differ somewhat from those in each of the others. No two liver cells, probably, are precisely alike in their chemical activities. In a single mucous membrane, the chemistry of the constituent gland cells differs markedly from the chemistry of the constituent nerve cells, connective tissue cells and smooth muscle cells. Within the channels of communication that carry fluids and solids about the great laboratory from work room to work room, chemical changes are constantly going on in the transported materials. Even the walls, the beams and the furniture of the billions of work rooms are themselves constantly undergoing chemical change. We are awed enough by the complexity of the chemical processes that go on in health; but let us not forget that in the diseased body, which is the province of the pharmacotherapist, this complexity becomes manifold. Into this apparently infinite welter of chemical transformations (though, in reality, orderly and ultimately knowable) goes the drug that the physician administers in the hope of curing, regulating or ameliorating. Its administration surely signifies courage on the part of the physician who has such a conception of the body's chemistry. The task he attempts is truly Promethean. Is it not to try "to defy Power, which seems omnipotent?"

## THE DEVELOPMENT OF PHARMACOTHERAPY.

Man's needs have been so urgent, however, that medical men everywhere, and at all times, have not hesitated to defy powers when they seemed malevolent; and drug therapy has, despite its besetting difficulties, become one of the successful methods by which medicine "folds over the world its healing wings."

The clinical experience of the centuries slowly supplied an important body of facts regarding the nature of disease and man's power to control it, but the formation of true guiding principles for pharmacotherapy had to await the rise of modern science. More of value has been learned regarding rational treatment by the use of drugs in the last fifty years, perhaps, than in all the centuries that preceded; for, during the last fifty years, we have gained entirely new conceptions of the nature and causes of disease.



Through chemical, physiologic, psychologic, pathologic and clinical studies we have learned much regarding pathogenesis, that is to say regarding the chains of changes in the body that follow on injuries of various sorts. Synthetic chemistry has supplied us with a host of new substances for trial as remedies. The new sciences of pharmacology and toxicology have revealed to us the mode of action of drugs and poisons, and medical students are observing for themselves, in our pharmacologic laboratories, the physiologic effects that follow the introduction of foreign substances into the animal body, and they measure some of these effects with instruments of precision. Knowing only too well that, in the diseased body, drugs often act in an unexpected manner, in ways very different from those in which they act in the healthy body, clinicians have wisely seen that the pharmacology of the laboratory, though of great value for the general advance of scientific therapy, cannot take the place of accurate clinical observation. It can do much to guide therapeutic effort and to supply criteria for judging of its effects, but the final and crucial test of the value of any therapy is that of actual clinical experience. The clinic can help the laboratory, and the laboratory the clinic; but each has its independent domain that should be conscientiously worked and zealously safeguarded.

#### THE NEW EXPERIMENTAL SCIENCES.

Recently, laudable attempts partially to bridge the gap between the pharmacologic laboratory and the clinic, in the interests of pharmacotherapy, have been observable in the work of the new sciences of experimental pathology and experimental therapy, especially experimental substitution therapy, and experimental antiparasitic therapy (immunotherapy, serotherapy and chemotherapy).

Workers in these new sciences reproduce certain sharply circumscribed syndromes in experimental animals and then study various forms of treatment experimentally, analyzing the effects of the measures tried. With the advent of experimental pathology and experimental therapy, we can hope for the rapid development of a systematic science of therapy; and though the transfer of results of experiments in treatment of sick animals to treatment of the sick human being will always mean a leap from the known to the unknown, still this transit will from now on be made with ever lessened danger. New drugs and chemicals will in the future be thoroughly

and reliably tested, not only in pharmacologic laboratories on healthy animals, but, as far as possible, also in laboratories of experimental pathology and therapy, on animals in which special diseases have been induced, before we shall feel justified in making trial of them in the treatment of sick human beings.

#### CLASSES OF PHARMACOTHERAPY.

Now that physicians generally understand that, in all diseases or pathologic processes, they have to deal with modifications of normal (or physiologic) processes that depend on definite disease causes, modifications, moreover, that are beyond the self-regulating capacity of the organism to keep within those limits of functional activity that we observe in "health," the internist can classify his pharmacotherapeutic efforts according to the kind of effect he desires to produce. Thus, (1) he may try with a drug to remove the cause of the disease or to render it harmless (etiologic pharmacotherapy); or (2) he may use a drug that will help directly to restore a pathologically disturbed function to normal (functional pharmacotherapy); or (3) he may administer substances that will aid the organism in its modes of reaction against the disease-cause (regulatory pharmacotherapy); or, finally, (4) he may employ drugs merely to relieve single troublesome symptoms (symptomatic pharmacotherapy). Internists who, after thorough and complete diagnostic studies, carefully consider these several indications (etiologic, functional, regulatory and symptomatic) should achieve in their pharmacotherapy the highest possible success.

#### ETIOLOGIC PHARMACOTHERAPY.

Pharmacotherapy is seen at its best when, through the use of a drug, the cause of a disease is removed or rendered harmless (etiologic pharmacotherapy) before the patient has sustained irreparable injuries. The organism can then right itself, so that its activities can resume their normal or physiologic course. As our knowledge of disease causes steadily undergoes increase, ever more maladies will be made accessible to etiologic therapy. Physicians of all times have considered the causal indication when they removed harmful substances from the stomach by emetics, such as mustard or ipecac, or from the intestine by purgatives, such as castor oil, calomel or magnesium sulphate. The greatest successes in causal therapy have,

however, been achieved by using drugs that kill living animal or vegetable parasites within the body, or that drive them from the body into the world outside. The use of oleoresin of male fern against tapeworm, of santonin against roundworms, and of oil of chenopodium against hookworms, are paradigms of antiparasitic pharmacotherapy. The parasites of malaria were killed by the quinin contained in cinchona long before we knew that the malarial fevers were parasitic in origin. Pathogenic amebas in the intestine can be killed off by means of emetin hydrochlorid. The fungi that cause blastomycosis and sporotrichosis die when subjected to the influence of the iodids. Noteworthy triumphs have recently been scored also by etiologic chemotherapy directed against certain parasites (trypanosomes, spirochetes and spirilla) that cause African sleeping sickness, syphilis, and relapsing fever. Through prolonged experimental work, parasitocides have been discovered that have a greater affinity for and toxic effect on trypanosomes and spirilla than on the body cells and organs; in other words, poisons that are more parasitotropic than organotropic can now be used to kill certain invading micro-organisms without too much injury to the invaded host. Arsphenamin and neo-arsphenamin help us greatly in the fight against syphilis, and are undoubtedly valuable additions to our pharmacopeia. With further studies of the parasitotropic qualities of various arsenical and antimonial compounds, we can reasonably hope for satisfactory means of control of a series of tropical diseases that up to recent times have defied the efforts of therapists.

In the antiparasitic treatment of diseases of bacterial origin, experimental chemotherapy has thus far been baffled. This does not mean, however, a permanent defeat. There is much to encourage investigators to continue their search for internal disinfectants that may be safely used. The body fluids and the body cells contain, and manufacture, substances that can kill bacteria. The chemical constitution of these bactericidal substances, we can feel sure, will ultimately be discovered; the substances will, later, be made synthetically and utilized in therapy. Moreover, toxic bacteriotropic substances that are foreign to the organism and innocuous for it will also doubtless be found and used. We already know that ethylhydrocuprein will kill pneumococci, though its deleterious effect on the optic nerve makes it unsafe as yet as a therapeutic agent. But who knows how soon some enterprising experimental chemotherapist may find a

related pneumococcidal substance that is less harmful to the body, just as the discovery of the relatively innocuous spirillocidal arsphe-namin succeeded that of the blindness-producing atoxyl?

#### FUNCTIONAL PHARMACOTHERAPY.

Though less ideal and important than etiologic therapy, much good can be accomplished by the internist who, making use of a so-called functional pharmacotherapy, tries to restore to normal some function that, through disease, has become disturbed or abolished.

This can easily be made clear by citing a few examples. Thus, a patient with valvular disease of the heart may get on well for years, thanks to the reserve force of his cardiac muscle. But, sooner or later, the function of the heart muscle begins to fail, and breathlessness, tachycardia, arrhythmia, passive congestion and edema appear. In digitalis, the pharmacotherapist possesses a remedy that, properly used, will often slow the heart rate and increase the contractility and tonicity of the muscular walls of the heart so that the circulatory insufficiency will disappear. Or, a patient in whom atrial (auricular) fibrillation exists may have the normal initiation and conduction of atrial stimuli restored by means of a few doses of quinidin. Or, again, a patient whose arteries are becoming sclerotic may have spasms of the coronary vessels and the severe pain of angina pectoris that can be relieved by dissolving a tablet of glyceryl trinitrate under the tongue, which, by dilating the pathologically contracted coronary arteries, removes directly a responsible functional disturbance. Similarly, we can relax the bronchospasm of a typical attack of bronchial asthma by the injection of a few minims of a solution of epinephrin (1: 1,000), and we can spur the atonic wall of the intestine to contract in a postoperative case by means of a hypodermic injection of solution of hypophysis (pituitary extract). In all these instances we make use of a functional pharmacotherapy.

Another example may be chosen from the field of metabolism. Thus, in gout, uric acid is not adequately excreted by the kidneys, being retained in the blood or deposited in the tissues about the joints. The function of uric acid excretion by the kidneys can be temporarily increased by the administration of cinchophen or neo-cinchophen, substances that also exert an exceptionally efficient analgesic effect in acute attacks of gout.

What we know as "organ therapy" may also be regarded as one kind of functional pharmacotherapy. If dried thyroids, for example,

be given to a patient with myxedema (due to absence or defective function of the thyroid gland), the substance administered is capable of substituting for the function in abeyance and, in turn, of restoring to normal function those distant organs whose activities have undergone change through lack of the thyroid hormone.

#### REGULATORY PHARMACOTHERAPY.

Turning next to regulatory pharmacotherapy, that form of treatment in which we administer remedies with the object of "aiding the body to react against the disease-process or the disease-cause," a good example will be seen in the pharmacotherapy of acute nephritis. In a severe glomerulonephritis, water, salt and urea are no longer adequately excreted by the kidneys, being retained in the body. The body attempts to excrete these vicariously, through the digestive tract and the skin. The physician may aid this natural reaction of the organism by using (1) a drastic purgative, like compound powder of jalap, which produces copious watery evacuations, and (2) a powerful diaphoretic, like pilocarpin nitrate, which causes free sweating. Such purgation and diaphoresis support the activities of the normal regulatory mechanisms of the body and are therefore classed as examples of "regulatory" pharmacotherapy.

In the treatment of diphtheria with antitoxin, we also employ a regulatory therapy, for, on injection of the antitoxic serum, we support the normal reaction of the organism in its effort to produce chemical substances that neutralize the toxins of the diphtheria bacilli.

The treatment of a posthemorrhagic anemia by preparations of iron may serve as a third example of regulatory pharmacotherapy. The body reacts after severe hemorrhage by increased activity of the red bone marrow, regenerating red blood corpuscles rapidly. More iron may be required for this accelerated erythropoiesis than is available in the ordinary diet. The reactive regenerative process can be strongly favored by administering ferrous carbonate, say in the form of Bland's pills.

#### SYMPTOMATIC PHARMACOTHERAPY.

Symptomatic pharmacotherapy, which neither intervenes in the disease process as such nor attacks its cause, is, however, a form of therapy that is by no means to be despised. Though it is directed

only toward single symptoms that injure or torment him, this therapy is highly important for the patient, and, when successful, is the ground for much gratitude on his part. There is scarcely a symptom that is complained of by patients that physicians have not attempted to influence by pharmacotherapeutic methods. And the relief that can be afforded in many instances thoroughly justifies the attention that is given to the *indicatio symptomatica*.

It is above all in the relief of pain and of various forms of mental and bodily discomfort that this is true. We would not willingly neglect the administration of morphin in renal colic; of acetylsalicylic acid in the arthralgias; of wine or beer to paralyze certain pathologic inhibitions and to bring needed relaxation; of heroin and codein in the racking cough of pneumonia; or of the various analgesics that are effective in migraine, in neuralgias, and in the lancinating pains of tabes. Though we may deplore the abuses of alcohol as a beverage, of purgatives in habitual constipation, of sedatives in the neuroses, and of hypnotics in insomnia, we all will admit that after causal, functional, and regulatory indications have been as fully met as our science permits of, there will be occasions when the merely symptomatic indication dare not be ignored.

#### CONCLUSION.

It will be clear from what I have said that the internist looks on the use of drugs in therapy more hopefully now, perhaps, than ever before. Available drugs are of real value in curing, in ameliorating and in preventing disease, and new drugs that are useful are steadily being discovered.

Adequately to make use of the pharmacotherapeutic means at his disposal for meeting etiologic, functional, regulatory and symptomatic indications, the internist must, it is true, have mastery over a large body of facts. He must be well trained in normal and pathologic physiology and should have become acquainted with the known facts of etiology and pathogenesis. He should have learned in the pharmacologic laboratory the effects of the more important drugs on the normal animal body; and he should have had opportunity in the hospital wards, and in the laboratory of experimental pathology and therapy, to observe the changes that can be produced by drugs in disease. Very few have as yet had opportunity for the latter, but the medical schools should provide for it in the future.

Our teaching hospitals at present are, perhaps, more diagnostic institutes than institutes of therapy. It might, possibly, be wise to divide our medical clinics into two parts, patients entering one division for general diagnostic study and emergency measures, to be transferred afterward to the other division for full treatment, the effects of which could be carefully observed by the students.

The internist with such a training in the medical school as I have outlined will be prepared to institute a rational therapy wherever this is possible. He will know how to make a judicious use of empiric therapy when a rational foundation is lacking. As a matter of fact, pathology and therapy have of late years made such rapid strides that the physician can, in the majority of instances, give reasons for the therapeutic faith that is in him. For this we have to thank both the research activity of the scientific laboratories and the keen and critical observations of our better clinics.

The introduction of new therapeutic methods and new drugs can scarcely be expected from now on to be arrived at by accident, or through pure empiricism. Every new therapeutic agent should, as Magnus<sup>1</sup> has emphasized, be thoroughly tested in the laboratories as regards its activity and its dangers and, later, in the organized clinics, before it is introduced into general medical practice. But results in clinical experience must ever remain the final and crucial test of every form of therapy.

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## THE DETERMINATION OF TANNIN.\*<sup>1 2</sup>

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A rather widespread controversy has arisen over a new method of tannin analysis described by the authors in two previous papers,<sup>3</sup> in which it was shown that the methods adopted as official both here

<sup>1</sup> Magnus, R.: *Allgemeine Pharmakotherapie*, in Krause and Garrè: *Lehrbuch der Therapie der inneren Krankheiten*, Jena 1: 71-143, 1911.

\*Reprinted from the *Journ. of Ind. and Eng. Chem.*, September, 1921.

<sup>2</sup> Received July 26, 1921.

<sup>3</sup> To be presented before the Leather Chemistry Section at the Sixty-second Meeting of the American Chemical Society, New York City, September 6 to 10, 1921.

<sup>3</sup> *Journ. Ind. and Eng. Chem.*, 12 (1920), 465, 1149.

and abroad are greatly in error, exceeding 200 per cent. in some cases. Changing a method of analysis upon which millions of dollars of tanning materials are bought and sold annually is admittedly a serious matter. Were the new method to supplant the old in the sale of extracts, drastic price changes would have to be made and many extracts would no longer hold their present relative standings or reputation as to tanning value. Since the official methods have been clearly proved unreliable, it would seem that the new method must now be tested generally to determine whether or not it will meet all the conditions that ought to be required of a method so important. Until now its use has been restricted because the procedure as originally described was both cumbersome and time consuming, all of the first efforts having been directed exclusively to devising an accurate method. But the procedure has since been developed until it is now quite as simple as that of any method in general use. In this paper we describe the simplified procedure, and also refute the objections which have been raised against the new method.

#### DEFINITION OF TANNIN.

A thorough review of the literature shows that it has been generally agreed to class as tannin that portion of the water-soluble matter of certain vegetable materials which will precipitate gelatin from solution and which will form compounds with hide fiber which are resistant to washing. Much confusion would have been avoided in discussion by making it clear whether the criticism was directed against the definition or the method.

#### CHANGES IN PROCEDURE.

In the method as originally described, the tanned hide powder had to be washed by shaking with water for 30 min., squeezing through linen, and repeating with fresh water until free from soluble matter, which usually required about twelve washings. This is now accomplished with very little effort in a washing apparatus to be described later. The washed powder, after drying, was analyzed for water, ash, fat, and hide substance ( $N \times 5.62$ ), and the percentages of these subtracted from 100 gave the per cent. of tannin in the powder. It was suggested earlier that this figure might be obtained simply by noting the increase in weight of the dry powder after tanning and washing, provided the washing operation was



so conducted that no powder was lost, making the determination direct instead of by difference and increasing the accuracy for unskilled analysts. The new washing apparatus not only makes this possible, but reduces the amount of hide powder required for a determination to one-sixth.

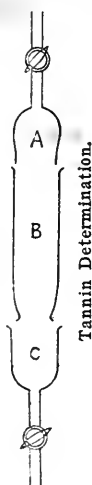
#### PRESENT PROCEDURE.

A solution of the tanning material is prepared of such strength that 2 g. of hide powder will detannize 100 cc. in 6 hrs. of shaking. With a little experimenting, safe limits are easily determined for all ordinary materials so that the need for repetition will be rare. For the extracts used in this work, suitable concentrations in grams per liter are 20 for hemlock, larch, oak, and sumac, 16 for gambier, and 7 for solid quebracho. The solution must be freed from insoluble matter, which may be done in the usual manner by adding kaolin, filtering through a thin paper, returning the filtrate to the paper for an hour to tan it, then discarding all liquor which has touched the paper, pouring fresh liquor on to the filter and collecting when the filtrate comes through clear. For materials which filter with difficulty, time can be saved by setting up several filters at one time. Standard hide powder,<sup>4</sup> or its equivalent, is extracted with chloroform to remove all extractable matter, and is then freed from solvent and stored ready for use. This treatment is chiefly to remove fatty matters, and it may be found convenient to treat a year's supply at once. Two grams of this powder, of known moisture content, are put into a 6-oz., wide-mouth bottle, 100 cc. of tan liquor are added, and the whole is put into a rotating box and shaken for 6 hrs. It is advisable to keep the liquor and wash water cool to guard against any tendency towards decomposition of the untanned portion of the hide powder. This matter requires attention only in hot weather.

The essential part of the washing apparatus is shown in Fig. 1 and consists of three glass parts fitting tightly into one another by means of ground joints. A small piece of fine filter cloth is stretched tightly over the bottom outlet of part B and is firmly secured by winding and tying strong thread around the groove. Parts B and C are then put together and the stopcock is opened. The tan liquor and hide powder, after the 6-hr. shaking, are washed into part B, the

<sup>4</sup> Prepared by the Standard Mfg. Co., Ridgway, Pa.

liquor being allowed to run through the open cock into a beaker and returned until reasonably clear.<sup>5</sup> The stopcock is then closed and B is half filled with water and then fitted to part A with stopcock closed.



The remaining part of the washing apparatus is a reservoir of water set high enough from the table to exert a pressure equal to a column of about 4 ft. of water upon the glass receptacle, which is connected to the reservoir by means of a rubber tube attached to A. The stopcock in A is opened wide, and the rate of flow of water is regulated to about 500 cc. per hr. by means of the stopcock in C, which is connected to the drain. Since the washing is usually complete in about 12 hrs., it is convenient to start it just before leaving the laboratory in the evening so that it will be complete at the start of the next day. However, washing should not be stopped until the wash water is colorless and does not darken upon the addition of a drop of ferric chloride.

The powder is then washed on to a Büchner funnel and freed from as much water as possible by suction. It is then allowed to dry in the air over night, after which it is completely dried in a vacuum oven for 2 hrs., desiccated and weighed. It is returned to the oven and reweighed as a check against insufficient drying. The increase in weight of the dry powder represents the amount of tannin present in 100 cc. of the original tan liquor.

We have found it very convenient to have rotating boxes capable of holding twelve bottles each and cylindrical stands equipped with twelve washing devices each. Given twelve filtered liquors Monday morning, the powders would be tanned and ready for washing before evening, ready for drying next morning, and the tannin values available before noon Wednesday. With one such outfit an analyst can easily complete twelve determinations every day and still have time for other work.

<sup>5</sup> This liquor must always be tested for tannin by adding one drop at a time, a freshly prepared solution of 10 g. gelatin and 100 g. sodium chloride per liter. A precipitate indicates that tannin is present, in which case the determination must be repeated, using a more dilute solution of the tanning material.

## COMPARATIVE ANALYSES.

The analyses of six typical extracts given in Table I show that there is practically no difference in results obtained by the original and revised procedures of the new method. Analyses by the official method of the American Leather Chemists Association, widely used in this country, are given for comparison.

TABLE I—COMPARATIVE ANALYSIS OF EXTRACTS BY A. L. C. A. METHOD AND THE ORIGINAL AND REVISED PROCEDURES OF THE NEW METHOD.

EXTRACT	Water	Insoluble	Non-tannin	Tannin (By Difference)	NEW METHOD	
					Original Procedure (By Difference)	Revised Procedure (Direct)
Gambier .....	48.84	7.58	15.78	27.80	7.32	7.44
Hemlock .....	51.76	7.32	15.04	25.88	16.38	16.39
Larch .....	51.63	5.41	20.00	22.96	12.70	12.82
Oak .....	53.51	2.55	18.35	25.59	11.63	11.42
Quebracho .....	19.41	9.50	6.86	64.23	44.33	44.03
Sumac' .....	49.44	2.86	22.56	25.14	13.10	13.04

## DISCUSSION.

A common objection to the new method has been that it appeared inconceivable that leather chemists everywhere should have been so misguided as to accept as official a method liable to a 200 per cent. error. The fallacy in the argument put forward lies in its assumption that leather chemists everywhere have found the official methods to be borne out quantitatively in practice. When data were called for to prove this assumption, apparently none were available. On the contrary, we have been able to secure data from both upper and sole leather yards showing that the amount of tannin appearing in the finished leather is very much less than entered the yards according to the A. L. C. A. method; and that the apparent loss of tannin corresponds closely to the difference in tannin content of the extracts as determined by the new and official methods.

After some experimenting with the new method, Schultz and Blackadder<sup>6</sup> raised a number of objections to it. Their first was that it was difficult to obtain concordant results, which they explained as being due in part to the fact that the tannin was determined by difference and was subject to the errors involved in determining the water, ash, fat, and hide substance in the tanned powder. This appears to us rather a matter of skill in manipulation, but in any event the cause has vanished with the revision of the procedure.

<sup>6</sup> *J. Am. Leather Chem. Assoc.*, 15 (1920), 654.

Their second objection was that the detannized liquor and wash waters gave a test for tannin when concentrated to small bulk. In an earlier paper <sup>7</sup> we showed that certain nontannins are converted into tannin when their solutions are evaporated and that this transformation can be followed by means of the new method, but not by the A. L. C. A. method.

Their third objection was that the degree of subdivision of standard hide powder is not uniform, that the finer portions become more heavily tanned but are more easily lost during the washing operation or in later handling, thus tending to give low results for tannin as a result of making the analyses on the portions of powder less heavily tanned. In the revised procedure no loss of powder during the washing is possible, and all of the powder is weighed after drying. It is worthy of note, however, that the results we obtained by the original and revised procedures are practically identical.

Schell <sup>8</sup> has raised an objection to the method that involves the definition of tannin. Following the work of Meunier, <sup>6</sup> he conceives the existence of two kinds of tannin which may be likened to quinone and hydroquinol. Meunier showed that quinone has tanning properties, while hydroquinol apparently has none. Given plenty of access to the air, however, solutions of hydroquinol become capable of tanning because of oxidation. According to Schell, the new method determines only the quinone-like tannin and fails to include hydroquinol-like bodies.

But hydroquinol admittedly has no tanning properties. It seems to us that the method is all the more accurate for not including as tannin, those bodies which are not tannin, although convertible by oxidation or otherwise into tannin. The existence of these substances in tanning materials has been recognized and discussed in our last paper, in which it was shown that the tannin content of a tan liquor is increased by boiling. There is good reason to believe that the new method can be developed to determine the amount of substances convertible into tannin as well as of actual tannin. This might be done simply by analyzing the liquor both before and after some special treatment, such as oxidation, that will convert into tannin all substances capable of such conversion. However, the data available to us indicate that only a fraction of these substances really appear as tannin in the finished leather.

<sup>7</sup> *Journ. Ind. and Eng. Chem.*, 12 (1920), 1149.

<sup>8</sup> *Le Cuir*, 9 (1920), 491.

<sup>6</sup> *Chimie & industrie*, 1 (1918), 71.

Schell is right in insisting that these nontannins have a value which should be recognized in judging the value of an extract, but the values should be recognized also of those substances which aid in the diffusion of the tannins into the hides and the sugars which form the necessary acids. Two extracts of apparently the same tannin content may have very different properties. The tannin content alone is no sure guide to the value of an extract; much importance is attached to the reputation of the extract manufacturer. It is not improbable that it will eventually be found preferable to sell extracts on a basis of total solid matter, leaving the extract men to compete with each other in establishing a reputation for producing extracts of high quality and constant composition.

In speaking of hydroquinol-like bodies, Schell implies the suggestion that what the official method really determines is the sum of these and the true tannins, but this is not so. Gallic acid belongs to the class of nontannins capable of conversion into tannin, but when added to a tan liquor only a variable fraction of it appears as tannin by the A. L. C. A. method, which makes the method quite unreliable and often very misleading. This is strikingly shown with gambier extract. The method calls for 12.5 g. of dry hide powder to detannize 200 cc. of tan liquor, which amount was assumed to be correct because the nontannin filtrate gave no test with the gelatin-salt reagent. Using this method on a gambier extract we found 26 per cent. tannin. But we then reduced the amount of hide powder to 1.5 g.; the nontannin filtrate gave a negative test with the gelatin-salt reagent, but the per cent. of tannin found was only 13. The extract is listed as containing 26 per cent. tannin simply because a group of men were more favorably disposed to make 12.5 g. of hide powder official than some other amount. This is treated more fully in our first paper.

The A. L. C. A. method is based upon a principle often employed in absorption experiments. It falsely assumes that the decrease in concentration of a tan liquor upon shaking with hide powder is a measure of the tannin content and that the solution absorbed by the substance of the hide is of the same composition as the remaining liquor. Thomas and Kelly<sup>10</sup> have shown to what ridiculous conclusions this can lead. In studying the effect of concentration of chrome liquor upon the adsorption of its constituents

<sup>10</sup> *Journ. Ind. and Eng. Chem.*, 13 (1921), 31.

by hide substance, they had occasion to use very strong liquors. Hide powder was treated with a chrome liquor containing 14.75 g. of chromic oxide per liter, but after 48 hrs. the concentration had *risen* to 15.40 g., although the hide powder had actually removed chromium from solution. This would correspond to a negative value for tannin by the A. L. C. A. method. What happened was that the hide powder absorbed a solution more dilute than the remaining chrome liquor and therefore concentrated the liquor more than enough to offset the chromium removed by combination with the hide substance. It is quite clear that one cannot determine the amount of matter removed from solution by noting the decrease in concentration of the liquor and calculating according to the instructions of the A. L. C. A. method.

#### SYNTHETIC TANNINS.

A representative of a firm manufacturing synthetic tanning materials of the Neradol type informed us that the use of the official method on their product meant nothing as it could be made to give any results desired. He was anxious to learn if the new method would indicate the per cent. of matter capable of forming a stable compound with hide substance. While we have done no work with syntans, as they are called, it is obvious that they differ from ordinary tan liquors in that they usually contain a large amount of free sulfuric acid. In using the new method on such materials there is the possibility that the acid might cause the hide substance to swell considerably during washing. This would slow down the washing action and tend to favor decomposition of hide substance, with a consequent loss in accuracy of the method. It seems possible that this might be avoided by using tap water saturated with salt for the first washings, until all sulfuric acid was removed, and then completing the washing with distilled water.

#### SUMMARY.

A modification of the authors' new method of tannin analysis is described which results in a great saving of time and labor, and tends towards increased accuracy.

Objections raised against the new method are refuted.

It is shown that the principle underlying the present official methods is unsound.

A suggestion for using the new method with syntans is made.

## NOTES ON ANCIENT MEDICINE.\*

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The science of medicine had its beginning in the mists of antiquity, and, in the absence of recorded facts concerning the very early times, it is not surprising that a mythology should have been developed with fanciful tales regarding such imaginary individuals as Apollo, Æsculapius, and Chiron. We know that the Egyptians transmitted to the Greeks much of the science they had used with advantage in the healing of the sick and wounded. Oracles were supposed frequently to indicate cures for diseased conditions, and temples were often places for the exchange of medical information; the priesthood of Greece caused tablets, certifying to cures, to be suspended in the temples where he that suffered might learn what had bettered the condition of another with a like affliction. Available literature tells us also that much was learned in early times by watching animals when laboring under disease: The goats of Crete are credited with having indicated the healing power of Dictamnus (wild marjoram); dogs, when indisposed, were noticed to seek *triticum repens* (couch grass—dog grass), and men were thus led to apply this drug to treatment of bladder inflammations; to the behavior of dogs mankind can also trace the first acquaintance with and use of purgatives; sheep known to have liver worms sought saline substances; cattle suffering from dropsical conditions were found to be benefited by drinking chalybeate waters; the hippopotamus is supposed to have taught the operation of phlebotomy (blood-letting), how, we are not informed; and from the sacred bird of Egypt, the ibis, the usefulness of enemata was learned. Among the Chaldeans and Babylonians a sick man was carried to a roadside where the passer-by might see him and tell what worked a benefit in the like condition in himself, his neighbor, his friend, or his aunt. It would appear that, in this respect, the ancients were pretty much like the people of today.

Much that is myth and fable concerning the science exists, but the first actual history goes back no further than the fourth century B. C. Hippocrates, a native of Cos, is thus the fountain head

\*From the *Supplement to the Naval Medical Bulletin*.

of all knowledge of medicine. The works of others who may have written before his time do not exist, and it is a further fact that all writings on medical subjects from the time of Hippocrates to the founding of the school at Alexandria by Serapion and Philinus, in the third century B. C., have also vanished; the school referred to is itself known only by references to it in other literature.

Then followed many writers on medicine and related sciences, some of whom were not physicians, so that the literature is clogged with "views" of persons who could not write with authority. To one going over some of the literature it seems that every philosopher felt himself capable of settling definitely mooted questions in medicine and, further, that every one who could write at all deemed himself a philosopher. It would be impossible in the scope of this paper to give a chronology noting the more important writers of ancient times on medical subjects; it should suffice to indicate in the proper places the times at which they lived.

Differences of opinion early led to the formation of several medical sects, the more important of which may briefly be noted here. The Dogmatici were apparently the parent-stock of our beloved allopaths of today; they approached the study of medicine in a truly scientific manner and later on more will be said concerning their division of the subject. Opposed to the Dogmatici were the Empirici and they were the first to cut into the practice of the "regulars." They founded the school at Alexandria, basing their teachings on what they termed The Tripod of Medicine, which consisted of observation (or autopsy), history, and analogy. Observation included what the practioners noted during the course of an illness, history contemplated the written notes left by other writers in like conditions, and analogy or the substitution of one thing for another, was what they were thrown back upon when called to treat a case in which there was no precedent to follow, and the indications were obscure. Sagacity and sound judgment contributed greatly to the success of this sect, they had only to combat the vague, half-baked theories of the regulars, but their rejection of the study of anatomy, physiology and pathology made of them simply high-class experimentalists. Three of the followers (or leaders) of this sect, Sextus, Marcellus, and Plinius Valerianus, have left writings. As Marcellus lived in the fourth century A. D., the sect existed at least 600 years. Ignorant and indiscriminate experimenting is blamed as the cause for



their downfall, and the term empire eventually became a word of reproach. The Methodici, of whom Themison in the first century B. C. was the founder, attempted to steer a middle course between the two sects previously mentioned. Caelius Aurelianus was the principal writer of this sect and his book on acute and chronic illness is one of the most valuable of antiquity. The Episyntheticici appear to have been a branch of the Methodici, which adopted for their own the best opinions of the other sects. It was founded about the year 100 A. D. by Agathinus of Sparta, and his pupil, Archigenes, is the father of the Eclecticici. We are not informed as to the doctrines of the latter sect but they probably attempted to reconcile the tenets of the older sects.

Besides the school at Alexandria already mentioned, others were established at Cyrene in Africa, Crotona, Cnidos, Rhodes, and Cos. The latter is the most famous, as this town was the birthplace of Hippocrates, and from the school came many of the most eminent ancient physicians.

Before going into the subject of medicine it is well to note that the physicians and surgeons of early days had their troubles. There was, to speak mildly, a great deal of diffidence regarding the use of medicines at all, and often bitter antagonism. The physician had not only to develop a science from nothing, but it was also necessary to educate the public into the view that he was a real benefactor to society. Some of the antagonisms may be noted in the quaint and sometimes fanciful phraseology of sixteenth century English. I quote from Burton:

"'Twas Plinies (first century A. D.) dilemma of old—every disease is either curable or incurable, a man recovers of it or is killed by it; both wayes physick is to be rejected; if it is deadly it cannot be cured; if it may be helped, it requires no physician; nature will expell it of it selfe."

"Plato (fourth century B. C.) made it a great signe of an intemperate and corrupt commonwealth, where lawyers and physicians did abound; and the Romans distasted them so much, that they were often banished out of their city, as Pliny and Celsus (contemporary of Pliny) relate, for six hundred years not admitted. It is no art at all, as some hold, no not worthy the name of a liberall science \* \* \* 'tis a corrupt trade \* \* \* no profession; the beginning, practice and progress of it, all is naught, full of imposture, uncertainty, and doth generally more harm than good. The divel

himself was the inventor of it." Shaw, in his preface to "The Doctor's Dilemma," was not more hypercritical.

"Much emulation, imposture, malice there is amongst them (physicians); if they be honest and mean well, yet a knave apothecary, that administers the physick and makes the medicine, may do infinite harm, by his old obsolete doses, adulterine drugs, bad mixtures. \* \* \* But it is their ignorance that does more harm than their rashness; their art is wholly conjecturall (if it be an art), uncertain, imperfect, and got by killing of men: They are a kind of butchers, leeches, men-slayers; chirurgeons and apothecaries especially, that are indeed the physicians, hangmen and common executioners; though to say truth, physicians themselves are not far behind."

Thus while Burton quotes his authorities he is quick to make it plain that he does not always accept their points of view: "But I will urge these cavilling and contumelious arguments no further lest some physician might mistake me, and deny me physick when I am sick; for my part, I am well perswaded of physick; I can distinguish the abuse from the use in this and many other arts and sciences; wine and drunkenness are two distinct things."

Archagathus, who lived in the latter part of the third century B. C., was the first foreign surgeon to settle in Rome. At first he was well received, a shop was provided for him, and he was given the honorable title *Vulnerarius* (healer?). However, on account of the frequency with which he used knife and cautery, the Romans soon changed his title to *Carnifex* (executioner).

The science of medicine was, by the Dogmatici, divided into anatomy and physiology, ætiology, pathology, hygiene, symptomatology (including diagnosis), and therapeutics, which also included pharmacy, surgery, and the regimen to be followed in illness which was contemplated under the division of dietetics. In the following an effort will be made to show by notes and quotations some of the conditions that existed in early days, which will present to the reader a means for calculating the enormous strides which have been made in the development of the science.

Alcmaeon, who lived about 540 B. C., was the first man who dissected animals; the dissection of the bodies of human beings did not come until a much later date. He is credited with having discovered the eustachian tube. He maintained that goats breathe

through the ear, and this belief is attributed to the supposition that the animal he was dissecting had had the ear drum destroyed.

Aristotle (fourth century B. C.) corrected the error of Alcmaeon, but had himself certain delusions. He says that the hearts has three ventricles, that there are but eight ribs on each side, and makes no distinction between the arteries and veins; he also believed the brain was not provided with a blood supply.

An old description divides the body into two parts, the "contained" and "containing." The contained consisted of four humors, *vis.*, blood, bile, water and mucus or phlegm, to which was sometimes added serum (from urine), sweat and tears. There was further an imponderable subtle vapor called spirits, which was supposed to be a "common tye or medium betwixt the body and soul." This view was accepted by Hippocrates, later with certain modifications by Galen, and, to a certain extent, in much later times.

I have before me a work written in 1621 which does not show a great deal of advancement on Aristotle. The description of the anatomy of heart and lungs is interesting: "The heart though it be a sole member yet it may be divided into two creeks, left and right. The right is like the moon increasing, bigger than the other part, and receives blood from vena cava, distributing some to the lungs to nourish them, the rest to the left side to ingender spirits. The left creek hath the form of a cone, and is the seat of life, which (as a torch doth oyl) draws blood unto it, begetting of it spirits and fire; and, as fire in a torch, so are spirits in the blood; and by that great artery called aorta, it sends vital spirits over the body; and takes ayre from the lungs, by that artery which is called venosa; so that both creeks have their vessels; the right two veins, the left two arteries, besides those two common ancractuious ears which serve them both, the one to hold blood, the other ayre for several uses. The lungs is a thin spongy part, like an ox hoof (saith Fernelius), the instrument of voice; annexed to the heart to express his thoughts by voice. \* \* \* That it is the instrument of voice is manifest in that no creature can speak or utter any voice that wanteh these lights. It is besides the instrument of respiration, or breathing; and its office is to cool the heart by sending ayre unto it by the venosal artery which vein comes to the lungs by that aspera arteria (trachea?), which consists of many gristles, membranes, nerves, taking in ayre at the nose and mouth, and it likewise exhales the fumes of the heart."

Other notes would tend to indicate that there was confusion between the nerves and ligaments, as well as between arteries and veins. The author from whom the above was quoted appears to have been more intent on perpetuating the quaintness from the ancients than disclosing the best thought of his time.

The division of the "contained" portion of the body into four humors led Hippocrates to develop what is known as the humoral pathology, in which it is postulated that the stomach is the prime source of the humors, and sickness is the result of their appearance in other parts. Invasion by bile caused acute diseases; mucus or phlegm was the cause of catarrh and the rheumatic affections; dropsy depended upon water from the spleen. The quantity of bile determined the type of fever. Beginning with an extreme quantity of bile, and lessening the amount, the fever would be called continued, quotidian or tertian; a quartan fever was one in which the bile was mixed with viscous black bile (or atrabile). Both Galen and Hippocrates believed inflammation to be due to the introduction of blood into a part which had none before. If this introduction was complicated by mucus, bile, or atrabile the inflammation would not be pure, but would be known as cedematous, erysipelatous, or scirrhus, respectively.

Surgery came to the Greeks from the Egyptians and, as in medicine, Hippocrates stands forth as the first writer of note. He is credited with ten works on the subject, though some of them are regarded as spurious. When one considers the defective state of the knowledge of anatomy, the success of this surgeon is remarkable. He was skilled in treating fractures and dislocations, and was also familiar with the trephine. Asclepiades (first century B. C.) was first to propose the operation of bronchotomy, though he never performed the operation. Ammonius of Alexandria was first to propose and perform a lithotripsy—stone in the bladder having been a popular malady. Celsus has minutely described the operation from whose description the following may be of interest: "A hook is to be insinuated behind the stone so as to resist and prevent its recoiling into the bladder, even when struck; then an iron instrument is used, of moderate thickness, flattened toward the end, thin but blunt; which being placed against the stone, and struck on the farther end, cleaves it." After Hippocrates, this Celsus is the next important writer on surgical subjects. Qualifications laid down by him for

a surgeon is evidence that the patient was required to possess considerable morale: "He ought to be young, or at any rate not very old; his hand should be firm and steady and never shake; he should be able to use his left hand with as much dexterity as his right; his eyesight should be acute and clear; his mind intrepid, and so far subject to pity as to make him desirous of the recovery of his patient, but not so as to suffer himself to be moved by his cries; he should neither hurry the operation more than the case requires, nor cut *less* than is necessary, but do everything just as if the other's screams made no impression on him." Galen was the most voluminous writer on surgical as well as medical subjects. He practiced surgery at Pergamus, but when he moved to Rome in 165 A. D. he confined himself to medicine, following, as he said, the custom of the place. He believed that the physician should not invade the domain of surgery save in actual emergency.

Blood-letting was a frequent practice, but there were many contentions as to the conditions under which it should be done. The phases of the moon and aspects of the planets were taken into consideration; the morning was the best time of day for this operation. Cupping (dry and wet), horse leeches, the cautery, and issues (seton) were respected surgical procedures. In regard to blood-letting Sallust Salvian says: "If the blood abound, which is discerned by the fulness of the veins, his precedent diet, the parties laughter, etc., begin with the median or middle vein of the arm; if the blood be ruddy and clear, stop it; but if black in the spring-time, or a good season, or thick, let it run according to the parties strength; and some eight or twelve days after open the head vein, and the veins of the forehead, or provoke it out of the nostrils, or with cupping glasses." However, "Before you let blood deliberate of it and well consider all the circumstances belonging to it." Hippocrates is quoted as saying: "In melancholy and mad men, the varicous tumor or hæmorrhoids appearing doth heal the same."

Something in the nature of a capital operation is indicated by the following: "Cauteries and hot irons are to be used in the suture of the crown, and the seared or ulcerated place suffered to run a good while. 'Tis not amiss to bore the skull with an instrument to let out fuliginous vapors." In another place the boring of the skull in two or three places is recommended as it "much availeth to the exhalation of the vapors."

Moderation in the use of medicines (or "physick") is emphasized by one writer: "A discreet and godly physician doth first endeavor te expell a disease by medicinall diet, then by pure medicine \* \* \* He that may be cured by diet, must not meddle with physick \* \* \* Whōsoever takes much physick in his youth, shall soon bewail it in his old age, purgative physick especially which doth much debilitate nature."

It was at one time an accepted theory that each locality provided a medicinal substance for each diseased condition occurring therein, and those who adhered to this theory objected strenuously to importing medicines from distant lands. By the terms "simple" was understood a single plant, or a medicine prepared from such a plant, while compounds were what the name indicates. Burton states that many people favor the "exotick simples," such as, "sena, cassia out of Egypt, rubarbe from Bombay, aloes from Zocotra, turbith, agarick, mirabolanes, hermodactils from the East Indies, tobacco from the West, and some as far as China, hellebore from the Anticyræ, or that of Austria which bears the purple flower."

In condemning the use of imported and strange drugs we note that, "Many an old wife or country woman doth often more good with a few well-known and common garden herbs, than our bumbast physicians, with all their rare, prodigious, sumptuous, far-fetched, conjecturall medicines." This would suggest a tendency to use European medicines in preference to foreign ones; nevertheless, the domestication of plants from distant lands was commended and practiced in the public gardens at Padua, Leyden, Montpelier, Oxford, and Nuremberg. This culture was approved in order that "the young students may be the sooner informed in the knowledge of them which, as Fuschius holds, is most necessary to that exquisite manner of curing, and as great a shame for a physician not to observe them, as for a workman not to know his tools."

Galeottus appears to have recognized some 800 simples including those classed as alteratives which he defines as remedies that "by a secret force and speciall quality, expell future diseases, perfectly cure those which are, and many such incurable effects."

The water lily was esteemed for its anaphrodisiac qualities, cabbage was thought to resist drunkenness and, "that which is more to be admired, that such and such plants have a peculiar vertue to such

particular parts: as to the head—aniseseed, foafoot, betony, calamint, eyebright, lavender, bays, sore, rue, sage, marjoram, piony, etc.; for the lungs—calamint, liquorice, enula campana, hysop, horehound, water germander, etc.; for the heart—borage, buglosse, saffron, bawm, basil, rosemary, violet, roses, etc.; for the stomach—wormwood, mints, betony, bawm, centaury, sorel, purselan; for the liver—darthspine, chamæpitys, germander, agrimony, fennell, endive, succory, liverwort, barbaryes; for the spleen—maidenhair, finger-ferne, dodder of thyme, hoppe, the rind of ashe, betony; for the joints—camomile, organ, rue, cowslips, centaury the less; and so on to particular diseases.”

Some notes regarding the identity of drugs used by the ancients may not come amiss:

Turbith is also known as turpeth and is the dried root and stem of *Ipomœa turpethum*. It is a purgative something like jalap but milder. It contains 10 per cent. of resin and a yellow coloring matter. It is said that the basic sulphate of mercury got its name “turpeth mineral” from its resemblance in color to the root.

Agarick is recognized as spunk touchwood or tinder, and is a fungus (*Polyporus officinalis*) growing on certain larches and pines, the best coming from Siberia. The active principle is agaric acid (agaricin) and, aside from the Solanaceous plants, is one of the best remedies we have for treatment of night sweats of phthisis.

Hermodactils was probably *Colchicum Illyricum*, or an allied species. It was also called Mercury’s finger, and was a root shaped like a heart, flattened, and of a white color.

Betony or betonica was named by Pliny from the Vettonese, a people of Spain, who discovered it. It belongs to the order Labiatae and has been used as emetic and purgative.

Eyebright also called euphrasia, is a small annual plant of Europe. It was formerly used in the treatment of affections of the eye, hence its name. It is mildly astringent.

Under the head of calamint, *Calamintha officinalis*, *C. nepeta*, and *C. sylvatica*, were included. Strongly aromatic, they were much thought of by the ancients.

Enula campana, or elecampane, is the *Inula helenium*, the plant supposed to have sprung from the tears of Helen. The root is stimulant and aromatic.

Agrimony was so named from the Greek word signifying “a

speck in the eye," which condition was supposed to be cured by the plant. It belongs to the rose family and is a bitter astringent.

Dodder is a parasitical plant of the genus *Cuscuta* and lives by attaching itself to clover, flax, thyme, and other plants.

Borage is identified as *Borago officinalis*, the stems of which contain potassium nitrate and some other salts.

Bugloss appears to be *Anchusa officinalis*, the root, leaves, and flowers of which were at one time recognized in our United States Pharmacopœia. They are practically devoid of medicinal properties.

Bawn is identified as the leaves and tops of *Melissa officinalis*, and is without medicinal value, though a highly flavored essential oil is contained.

Black hellebore, which was formerly official, we recognize as a drastic, hydragogue cathartic. It was first discovered (so the story goes) by a shepherd named Melonpodius, who noted the behavior of his goats after they had eaten it, and applied the rhizome (some say the milk from female goats which had eaten of the plant) to the treatment of illness in Elige and Calene, daughters of King Proteus.

The ancients used so many drugs which today we find inert and practically useless, it must appear that the apothecaries of those days had more ability in compounding medicines, or else the vehicles commonly used were potent and had therapeutic value. Here is a testimonial to the value of wine of bugloss, which reads not unlike some of our recently popular patent medicines:

"An excellent cordiall, and therefore worthily reckoned up amongst those herbs which expell melancholy and exhilarate the heart \* \* \* If taken steept in wine, if wife and children, father and mother, brother and sister, and all thy dearest friends should die before thy face, thou couldst not grieve or shed a tear for them."

Concerning a compound wine containing bugloss, borage, cinnamon, etc., it is stated, "It drives away leprosy, scabs, cleers the blood, recreates the spirits, exhilarates the mind, purgeth the brain of those anxious, black, melancholy fumes, and cleanseth the whole body of that black humour by urine. To which I add (saith Villanovanus) that it will bring mad men such as are raging bedlams, as are tied in chains, to the use of their reason again." The fourth ingredient appears to have added character to this compound.



Bawm was considered to "help concoction, to cleanse the braine, expell all careful thoughts and anxious imaginations."

Milady Nicotine comes in for extended consideration: "Tobacco, divine, rare, superexcellent tobacco, which goes so far beyond their panaceas, potable gold and philosopher's stones, a sovraign remedy to all diseases. A good vomit (emetic) I confess, a vertuous herb, if it be well qualified, opportunely taken, and medicinally used; but as it is commonly abused by most men which take it as tinkers do ale, 'tis a plague, a mischief, a violent purger of goods, lands, health—hellish, divelish, and damned tobacco, the ruine and overthrow of body and soul."

German frightfulness pales into insignificance before the story of Solon who, while laying siege to a certain city, "steeped hellebor in a spring of water which by pipes was conveyed into the town, and so poisoned or else made so feeble and weak by purging that they were not able to bear arms." Paracelsus also speaks of this drug and admired particularly the extract which he called, "The sole and last refuge to cure this malady, the gout, leprosy, etc."

If it were desired to marshal authorities on the use of wine in medicine, the ancient literature contains much material both for and against, though the objections were chiefly against excesses. Rhasis knew no better physic for a melancholy man and "he that can keep company and carous needs no other medicine." Avicienna, also an Arabian, goes further and advises the melancholy patient to drink and to "now and then be drunk; excellent good physick it is for this and many other diseases."

Another testimonial, this time to the efficacy of borage wine, will conclude this section: "My conscience bears me witness that I do not lye. I saw a grave matron helped by this means; she was cholerick and so furious sometimes, that she was almost mad and beside herself; she said and did she knew not what, scolded, beat her maids, and was now ready to be bound, 'till she drank of this borage wine and by this excellent remedy was cured which a poor forrainer, a silly beggar, taught her by chance, that came to crave an alms from door to door." It is to be deplored that before and after taking photographs are not available!

There was some difference of opinion as to the value of precious stones and minerals, and their application to the prevention and treatment of disease. In his tract against Paracelsus, Thomas Eras-

tus said, "That stones can work any wonders, let them believe that list; no man shall perswade me: for my part, I have found by experience that there is no vertue in them."

Potable gold, mercury, arsenic, and antimony were used to a certain extent, and Matthioli holds "No man can be an excellent physician that hath not some skill in chymisticall distillations, and that chronick diseases can hardly be cured without minerall medicines." Regarding antimony, a case is cited of a parish priest in Prague, Bohemia, who "was so far gone with melancholy that he doted and spake he knew not what; but after he had taken twelve grains of stibium (as I saw myself and can witness, for I was called to see this miraculous accident) he was purged of a deal of black choler \* \* \* yet it did him so much good that the next day he was perfectly cured."

Among the Romans who were high livers emetics were very popular and the taking of an emetic was frequently the prelude to a banquet.

Amulets and charms were much in vogue. Regarding the topaz it was said, "If it be either taken in a potion or carried about, it will increase wisdom, expell fear." Cardan brags that he hath cured many men with it which, "when they laid by the stone were as mad again as ever they were at first."

"In the belly (gizzard ?) of the swallow," says Burton, "there is a stone found, called chelidonium which, if it be lapped in a fair cloth, and tied to the right arm, will cure lunaticks, mad men, make them amiable and merry."

The carbuncle and coral were believed to "drive away childish fears, divels, overcome sorrows, and hung about the neck, repress troublesome dreams." Ruess ascribes the same qualities to the diamond.

Classified under precious stones are "the bone in the stag's heart," a "moncerot's horn," and the "Bezoar's stone." This latter is "found in the belly of a little beast in the East Indies" and "Rhodeus saith he saw two of these beasts alive in the castle of the Lord of Vitry at Coubert."

Among amulets, the following were guaranteed to give satisfaction: "A ring made of the hoofe of an asses right fore foot, carried about." The carrying of a spider in a nutshell wrapped in silk was thought "to keep off ague."

For epilepsy, "a piece of an old sailcloth taken from a ship-wrecked vessel, to be tied to the right arm for seven weeks together."

For colic, "The heart of a lark to be fastened to the left thigh."

For a quartan ague, "A few hairs taken from a goat's chin."

"Pliny says that any plant gathered from the bank of a brook or river before sunrise, provided that no one sees the person who gathers it, is considered as a remedy for a tertian ague when tied to the left arm, the patient not knowing what it is."

"A person may be immediately cured of the headache by the application of any plant which has grown on the head of a statue, provided it be folded in the shred of a garment, and tied to the part affected with a red string."

Not quite so fanciful, yet not without interest is a remedy for the flatulence occurring in "hypochondriacal melancholy." It consisted in the use of a clyster pipe connected to a pair of bellows, concerning which, Burton simply comments that nature abhors a vacuum.

This paper concludes with a note on the subject of dietetics. Burton enumerates practically all foodstuffs of all times and then proceeds to quote authorities condemning all of them. With regard to beer, he quotes Crato as objecting to it as "windy because of the hop," and translates Henricus Abrincensis:

"Nothing comes in so thick;  
Nothing goes out so thin;  
It must needs follow, then,  
The drugs are left within"—

References: *Dictionary of Greek and Roman Antiquities*, Anthon. *Anatomy of Melancholy*, Burton.

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#### MODE OF ACTION OF SOME COMMON LAXATIVES.\*

Without doubt the common laxatives are the most widely used drugs in the entire pharmacopœia of the modern physician; hence the conclusion is irresistible that he should be adequately informed regarding their precise mode of action. If an added reason were necessary it could readily be found in the all but universal use

\*From the *Journ. of A. M. A.*, August, 1921.

of laxative drugs by the laity. Sometimes they are purchased by the public with a distinct appreciation of their purpose; not infrequently potent laxatives represent an essential ingredient of proprietary and "patent" medicines that are secret as to composition and misrepresented with respect to their pharmacology. Probably physicians would be more discriminating, or at least more rational in the prescription of the various laxative preparations, if information regarding the pharmacodynamics of the subject were more widely disseminated among the members of the profession.

Calomel is a popular representative of the group of non-saline laxatives. It has currently been represented to act by promoting intestinal secretion and retarding absorption, so that an accumulation of the abundant fluid and a consequent evacuation of semisolid contents ensues.<sup>1</sup> A recent investigation of the pharmacologic action of calomel, aided in particular by roentgen-ray observations of the progress of the alimentary reactions has not substantiated the view just cited. Working in the pharmacologic institute of the University at Utrecht van der Willigen<sup>2</sup> has concluded that absorption in the gastro-intestinal canal is not interfered with in the presence of calomel. The drug functions by promoting more vigorous movements of the small and large intestines whereby the contents are propelled so rapidly toward the rectum that absorption and the production of formed stools cannot take place. The fundamental feature in the action of calomel therefore, is its influence on alimentary peristalsis.

The widely used phenolphthalein, the laxative action of which was an accidental discovery of pharmacology, is another drug which promotes peristalsis so that fluid contents are driven into the proximal colon more rapidly than under normal circumstances. Van der Willigen has recently demonstrated that the drug does not retard absorption, nor does it produce secretion in undue quantities, as is currently taught. In connection with this laxative also, then, our present day assumptions must be revised.

How sulphur acts to promote purgation has been considerably debated. One investigator, for example, has believed that it gives

<sup>1</sup> Meyer, H. H., and Gottlieb, R.: *Experimentelle Pharmakologie*, Ed. 4, Vienna, 1920.

<sup>2</sup> Van der Willigen, A. M. M.: *Die Abführwirkung des Kalomels*, Arch. f. d. ges. Physiol. 186: 185, 1921.

rise to sulphurous acid which acts as an irritant in the bowel. In contrast with this is the finding of hydrogen sulphid in the lower small intestine and upper large bowel after ingestion of sulphur. The most recent investigator van der Willigen has adopted the hypothesis of the function of the sydrone sulphid as the potent factor. He thus pictures its action: Ordinarily the chyme which discharges from the small intestine into the colon is soon concentrated there by the rapid absorption of water; but when hydrogen sulphid is formed in considerable abundance from ingested sulphur it provokes a more rapid passage of the semi-fluid contents beyond the colon so that the usual concentration cannot take place. A corresponding change in the feces is observed along with the more rapid evacuation.

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### THE POWER OF THE HEART.

A writer in the *Scientific American* has been doing some figuring as to the horse-power—he does not use this expression—of the human heart and he evolves some statistics which while of no practical importance, are interesting. Within each human breast, he says, this energetic organ is beating, on an average, about seventy-five times a minute, or 4500 times an hour. Accordingly, the heart beats, approximately 108,000 times daily, 39,000,000 times yearly, and, during a lifetime of three-score and ten years, two billion seven hundred million times. If we estimate the population of our world at 1,700,000,000 people, then all the human hearts on our terrestrial planet are beating at the rate of, approximately, 127,000,000,000 times a minute, or 66 quadrillion times a year. That is to say, these 1,700,000,000 human hearts are throbbing at a rate of about 2 billion times a second.

As we well know, our heart-engine contains four compartments, two auricles and two ventricles. The auricles are reservoirs which supply the pumping ventricles with blood. Therefore, the dynamic energy of the human heart resides in the right and the left ventricles. When these ventricles contract, the right ventricle sends its supply of impure blood to be purified by the oxygen in the lungs, and the left ventricle forces its supply of purified blood to circulate in the body. When the "heart beats," that is, when the right and left ventricles beat an average of about 10 cubic inches of blood

is expelled from the heart engine. Accordingly, in a minute, after seventy-five heart beats the energetic heart has pumped 750 cubic inches of blood. This means that the heart pumps 45,000 cubic inches of blood an hour, 1,000,000 cubic inches of blood a day, and 392,000,000 cubic inches, or more than 225,000 cubic feet of blood each year. Were the heart a water pump instead of a blood pump, it would expel since a cubic foot of water weights about  $62\frac{1}{2}$  pounds, approximately, 7000 tons of water, during the course of one year.

And this amount of work is accomplished by only a part of a small muscular organ about as big as the average human fist! It has been estimated that the left ventricle alone exercises sufficient pressure per square inch to support a column of blood 9 feet in height, and that it performs daily an amount of work equal to 90 foot-tons. Were we able to collect in a cubical reservoir all the blood pumped by one heart-engine in one year, that reservoir would be about 61 feet in each of its three dimensions. Or, were a circular water-tower with a diameter of 50 feet, it would be somewhat more than 115 feet in height, and it would contain about 1,700,000 gallons.

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#### ANTIDOTING MERCURIC CHLORIDE POISONING.\*

The following mode of treatment in the antidoting of mercuric chloride poisoning has been sanctioned and recommended by the Naval medical authorities, and is alleged to be certain of its aim if its instructions are rigidly adhered to. [Adherence to these specifications seem to require the services of an entire hospital staff.—Ed.]

1. Administer the whites of three eggs beaten up in a quart of milk and then empty the stomach by siphonage.
2. Give 300 cc. of fresh calcium sulphide solution, containing 1 grain to 1 ounce of water by mouth.
3. Wash out the stomach with fresh calcium sulphide solution, 1 grain to 1 ounce of water.
4. Administer in powder or tablet 0.36 gram of sodium phosphite and 0.24 gram of sodium acetate. If this is not available, give the following:

\*From the *Naval Medical Bulletin*.

Sodium hypophosphite .....	1 gm.
Water .....	10 mls
Hydrogen peroxide .....	5 mls

Use ten times as much of the hypophosphite as poison taken. Give a copious lavage of stomach with the above antidote diluted twenty times. Give the above undiluted antidote every eight hours for two days.

5. Pour through the stomach tube after the above lavage a solution of 3 ounces of sodium sulphate and 6 ounces of water containing 5 grains of calcium sulphide. Let these solutions remain in the stomach.

6. Give intravenously after withdrawing 600 cc. of blood, 800 cc. of Fischer's solution or of bicarbonate-glucose solution.

Fischer's solution:

Sod. chloride .....	14 gm.
Sod. carbonate .....	20 gm.
Aq. dist. ....	qs. 1000 cc.

7. Wash out the stomach morning and night, giving by the mouth after each washing 5 grains calcium sulphide dissolved in 3 ounces of water. Continue this lavage until the stomach washings are free from mercury when tested by Elliott's method and until the urine is free from mercury.

8. Give high colon irrigations of warm water morning and night, using 8 gallons of water for each treatment.

9. Give a hot pack twice daily.

10. Give 8 ounces of milk every second hour.

11. Give every second hour 8 ounces of the following solution, by mouth, alternating with the milk:

Potassium bitartrate .....	dr. j
Sodium citrate .....	dr. j
Sucrose .....	dr. j
Lactose .....	dr. iv
Lemon juice .....	oz. j.
Boiled water .....	oz. xvj

12. Force the patient to drink large quantities of the alkaline waters, such as Celestin Vich or Kalak water

13. Give a low fat and low protein or high carbohydrate diet

for four weeks. Avoid salt in diet, as it increases absorption of the mercury.

14. Give by continuous protoclysis a solution containing 1 dram of potassium acetate, 4 drams of glucose, and 3 drams of sodium carbonate to the pint.

15. Keep the urine alkaline to methyl red.

16. Continue rest treatment until recovery, usually a period of three weeks.

### HAINES MODIFIED TEST FOR GLUCOSE.\*

As far back as 1874, W. S. Haines<sup>1</sup> introduced a test for sugar in the urine which was regarded as more delicate than the methods in common use. Recently the same investigator, together with G. P. Pond and R. W. Webster,<sup>2</sup> published an improved test capable of detecting with certainty amounts about 0.03 per cent. of sugar, which is about the upper limit of the so-called "normal" sugar of the urine. That is, pathological sugar will be indicated, but physiological sugar will go undetected.

The composition of the improved Haines solution is:

Copper sulphate .....	5 gm.
Glycerin .....	250 cc.
Potassium hydroxide .....	20 gm.
Distilled water to .....	1000 cc.

The copper sulphate is dissolved in a mixture of the glycerin and an equal amount of water, with the aid of gentle heat. The potassium hydroxide should be dissolved in about 200 cc. of water and added to the copper solution with constant stirring, the whole being made up to volume with distilled water. This solution keeps indefinitely, although with many of the specimens of glycerin now obtainable on the market a reduction may be observed. If, however, the solution be allowed to stand in a warm place for forty-eight hours, the clear supernatant fluid may be decanted or filtered from the precipitated cuprous oxide, without impairing its delicacy.

\*From *The Prescriber*, 1921, p. 291.

<sup>1</sup> *Med. Examiner*, Dec. 1, 1874, p. 569.

<sup>2</sup> *J. Amer. Med. Assoc.*, Jan. 31, 1920, p. 301.



The glycerin increases the specific gravity of the solution, and thus admits of the test being applied as a contact reaction in the following manner: Heat 5 cc. of the solution to boiling in a test tube; then remove from the flame and hold at an angle of 40° and add carefully from a medicine dropper 10 to 20 drops of urine freed from phosphates as shown below. Place the tube in a rack and observe the reaction. If sugar is present in quantity exceeding 0.1 per cent., a brick-red or yellow ring appears at once at the junction of the two liquids. Less than 0.1 and over 0.03 per cent. will show a ring in from a few seconds to a minute; the smaller the quantity of sugar the longer will the ring take to form and the more yellow will be its color.

Before applying the test the urine should be freed from phosphates by the addition of a few drops of solution of KOH (5 or 10 per cent.), allowing the precipitated phosphates to settle. This makes the test more delicate and is necessary to obtain reliable results; when the proportion of sugar is high the reaction will appear without previous removal of phosphates.

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## REPORT OF THE SEMI-ANNUAL MEETING OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCI- ENCE, HELD AT THE COLLEGE ON SEPTEMBER 26, 1921.

The meeting was called to order by the First Vice President, Mr. Rohrman, at about three o'clock. The minutes of the previous meeting were read by the Secretary. Mr. Rumsey suggested that the resolutions presented by Mr. Wetherill at the last meeting be expunged from the minutes. Chairman Rohrman ruled that the resolutions referred to were a proper part of the minutes of the previous meeting in as much as they were adopted by a nearly unanimous vote of the members present at that meeting and that they should therefore be retained in the record. This ruling of the chairman stood and the minutes were approved as read.

The minutes of the Board of Trustees were then read by Mr. Beetem, Secretary to the Board. Mr. Osterlund moved that the minutes of the meetings of the Board of Trustees held on June 7

and August 24 as read at this meeting be and hereby are approved and the action taken at the said meetings be confirmed and adopted by the corporation. Dr. Mattison suggested that it was unnecessary to approve the minutes of the Board of Trustees if they are correct and accurate. Mr. Osterlund replied that his motion was in conformity with the college by-laws which require action by the college upon the minutes of its Board of Trustees. A vote was then taken on Mr. Osterlund's motion and carried by a large majority.

There was no unfinished business.

The following reports of committees were then presented:

Committee on By-Laws, by J. W. England, chairman, reported progress.

Committee on Resolutions to Retiring Officers, by J. W. England, chairman, reported progress.

Committee on Nominations, Mr. John K. Thum, chairman—in the absence of the chairman this report was read by the Secretary.

"To the Recording Secretary,

Philadelphia College Pharmacy and Science.

Dear Sir:

The Committee on Nominations submits the following names for the list of offices to be filled at the stated meeting of the Philadelphia College of Pharmacy and Science on the fourth Monday in September, 1921:

For President ..... William C. Braisted

For Board of Trustees—Five to be elected.

\*Richard M. Shoemaker, Ph. G. term expired.

Henry K. Mulford, Ph. G. term expired

Jacob M. Baer, Ph. G. term expired

George D. Rosengarten, Ph. D.

C. Mahlon Kline, Ph. B.

Walter V. Smith, Ph. G.

George B. Evans, Ph. G., to fill the unexpired term of Walter A. Rumsey, resigned.

Very truly yours,

JOHN K. THUM, *Chairman.*"

The Secretary then read letters of withdrawal as candidates for the Board of Trustees from Mr. J. M. Baer and Mr. H. K. Mulford.

\*In a note attached to the report the nominating committee submitted the name of Charles H. La Wall to fill the vacancy in the list of nominees occasioned by the death of Mr. R. M. Shoemaker which occurred subsequent to the first meeting of the committee.

Doctor Mattison moved that the name of Mr. Howard B. French be added to the report of the nominating committee as a nominee for the office of President of the College.

The Chair declared this out of order as no motion had been made that nominations from the floor be opened. The Chair stated it as his opinion that this privilege should be granted to any one desired to nominate from the floor and said that he would entertain a motion to that effect. Doctor Mattison then moved that nominations from the floor be opened. The motion was seconded by Professor La Wall and was carried unanimously.

Doctor Mattison placed in nomination the name of Mr. Howard B. French for President. The nomination was seconded by Mr. George M. Beringer.

Mr. Peacock moved that nominations be closed. This motion was duly seconded and carried.

Mr. George M. Beringer directed attention to the vacancy left by the resignation of the Treasurer of the College and moved that nominations be opened for Treasurer. Professor Stroup moved that nominations be reopened. The motion was seconded and carried. Mr. Beringer then placed in nomination the name of Mr. Milton Campbell for Treasurer of the College which was properly seconded.

Mr. Beringer stated it as his opinion that Mr. Osterlund was no longer a member of the Board of Trustees by virtue of his resignation from the office of President of the College, and moved that nominations for the Board of Trustees be reopened. The Chair stated that Mr. Osterlund was not functioning as an ex-officio member of the Board but that he had been regularly elected as a trustee of the College and had not relinquished that office. Mr. England stated that he had consulted the College Solicitor, Mr. McKaig, as to the legality of Mr. Osterlund's position on the Board and that the solicitor had confirmed the impression that Mr. Osterlund is a qualified member of the Board of Trustees by reason of his election thereto.

Mr. England moved that the body go into election of officers and members of the Board of Trustees. The motion carried.

Mr. Beringer stated that the custom of the College in recording the members present was not being followed and the Chair directed his attention to the fact that the members were being registered at that moment.

The Chairman appointed the following election officers: Messrs. J. J. Bender and J. N. G. Long as Tellers and Otto Kraus as Judge. Mr. England moved that as each member of the College voted his name on the membership list be checked off. This motion carried. Ballots were then distributed and the Chair directed attention to the fact that the name of Mr. Milton Campbell did not appear upon the ballots which had been prepared and should therefore be inserted by those voting.

At this juncture Doctor Mattison stated that he had had legal advice on the matter of Mr. Osterlund's status as a member of the Board of Trustees and as long as there was a question he desired to nominate Mr. Osterlund for membership to the Board. Chairman Rohrman declared the motion out of order. Mr. Beringer made an appeal from the decision of the Chair on the question. Chairman Rohrman stated that he had ruled that Mr. Osterlund is a bona fide member of the Board of Trustees. On motion, the ruling of the Chair was sustained by a large vote, a scattered few supporting the appeal from the decision.

In order to facilitate the election the Chairman was asked to appoint an additional member and Mr. Peacock was appointed to assist the other election officers.

Upon completion of the count of the ballots cast, the election officers presented the following report:

"We, the undersigned Judge and Tellers, appointed to conduct the election, at the Semi-Annual meeting of the members of the Philadelphia College of Pharmacy and Science, held on September twenty-sixth, nineteen hundred and twenty-one, report that votes were cast for the following persons:

For President:

Howard B. French,	15 votes
William C. Braisted,	146 "

For Treasurer:

Milton Campbell,	161 "
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For Trustees:

George B. Evans,	161 "
George D. Rosengarten,	161 "
C. Mahlon Kline,	161 "
Walter V. Smith,	161 "
Charles H. La Wall,	161 "

JOHN N. G. LONG, *Teller,*

JOHN J. BENDER, *Teller,*

OTTO KRAUS, *Judge of Election.*

OTTO KRAUS, *Notary Public."*

The election officers were properly sworn and the notarial seal attached to the report by Notary Kraus.

Following presentation of this report Chairman Rohrman declared the following gentlemen to be properly elected to fill the respective offices in the College:

President: William C. Braisted. Term expires March, 1922.

Treasurer: Milton Campbell. Term expires March, 1922.

For three-year terms as trustees:

George D. Rosengarten,  
C. Mahlon Kline,  
Walter V. Smith,  
Charles H. La Wall.

To fill the unexpired term of Walter A. Rumsey, resigned:  
George B. Evans. Term expires September, 1923.

The Chair appointed a committee consisting of Messrs. Osterlund, Blackwood and La Wall to proceed to the Bellevue-Stratford and escort President Braisted to the College.

Professor Cook, on behalf of the donors, presented to the College the following gifts which had been received during the summer from members and friends of the College. These consisted of:

From Mr. William A. Whittem, of Chestnut Hill, Pa.: A stone Mortar given to Mr. Whittem, many years ago, by Mr. Wetherill, of the paint firm.

A wooden Mortar and Pestle, which Mr. Whittem thinks was used during the Civil War in the hospital at Bungtown, now Wyndmoor, and which was given to him by the late Dr. William Moss, who, with Doctor Gross, was stationed at that hospital.

From Dr. J. B. S. Egee, South Hampton, Pennsylvania: An iron Mortar and Pestle.

From Mr. George B. Evans, Philadelphia, Pa.: A wooden Mortar and Pestle which Mr. Evans picked up in his travels.

It was moved that the thanks of the College be conveyed to the foregoing list of donors by the Secretary when acknowledging the receipt of the gifts.

Upon motion of Professor Stroup, duly seconded and carried, the Board of Trustees was instructed to take up with the proper authorities the paving of the street to lessen the noise.

Upon motion by Doctor Mattison, seconded by Doctor Robinson and carried, the Board of Trustees was instructed to consider the matter of placing double windows on the front of the building to keep out the street noises. Chairman Rohrman stated that the matter of paving the street had been taken up with the city authorities and that the Mayor had promised his support in the work.

At this juncture President Braisted, accompanied by the Committee of escort entered and Chairman Rohrman, in greeting him, said: "It is my pleasure to inform you that you have been elected to the Presidency of the College. You have made a reputation in your other fields of endeavor, and the present financial and physical condition of the College fully convinces us that your reputation is justified. You will have behind you a harmonious Board of Trustees and a no less harmonious faculty, who are not only willing, but eager to render their services to you and all that is within their power.

Before turning this meeting over to you I wish personally to wish you God-speed in your hopes for this College.

Members of the Philadelphia College of Pharmacy and Science, our President."

In assuming the Chair, Doctor Braisted said:—

"Members of the College, from the remarks of the Chairman, Mr. Rohrman, I take it that after your careful deliberations of this afternoon and with due consideration from all points of view you have elected me to be your president I want to express to you my full appreciation of the high honor conferred on me by this action and to thank the Chairman for his splendid words of assurance of support from the College as a whole, from the Board of Trustees and the officers and faculty of the institution—I shall need your help, advice and assistance in the months to come in the great work before us and it is my view that no policy or action affecting the College or the profession of Pharmacy shall be taken by me without the hearty approval and direction of the various bodies concerned.

"I should love to discuss here today, at length the many issues before us but feel that the hour is so late that I may not trespass further on your time and patience.

"The first step in the work, the rehabilitation of the building and the expansion of the Educational programme has been accomplished during the past summer. How successfully this has been done and how it has been accomplished is known to you and the evidence of

the work done meets your eyes on every hand. No further reference to this is needed by me. Much time and thought has been and will be given to the remainder of the work including the future of the College, the raising of funds, the promotion of the interests of Pharmacy as a major science and profession, the closer relation of Pharmacy and Medicine and you will be kept informed as the work progresses and at the proper times of contemplated and accomplished work. When the extent of the work is reviewed involving as it does so many difficult and delicate problems I confess to some degree of apprehension as to my ability to carry out the part of the programme you have given me—but if we can have happy, kindly, interested and hearty co-operation by our entire body, we may achieve results far beyond our most sanguine hopes and the future of this splendid institution may ever transcend, in usefulness and splendid humanitarian work, and the record of the past of which we are all so proud. I thank you gentlemen for your confidence in me and shall do the best I can to deserve your approbation and to carry to a successful issue your desires and hopes in the profession that you honor.”

Following prolonged applause the meeting adjourned.

AMBROSE HUNSBERGER, PH. G.,  
*Recording Secretary.*

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## SCIENTIFIC AND TECHNICAL ABSTRACTS

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CARBON MONOXIDE POISONING IN CLOSED GARAGES.—In this article attention is called to the fatalities occurring as the result of inhaling carbon monoxide from the exhaust gas of automobile engines running in small, closed garages. As this is not an infrequent item of news in the winter months, the public, particularly automobile owners and garage workers are warned of the danger in running a gasoline engine in a small, unventilated space.

In connection with experiments having to do with the problem of ventilation involved in the proposed vehicular tunnel under the Hudson River, several interesting facts have been demonstrated.<sup>1</sup>

<sup>1</sup>Physiological Effects of Automobile Exhaust Gas and Standards of Ventilation for Brief Exposures. Yandell Henderson, Howard W. Haggard, Merwyn C. Teague, Alexander L. Prince and Ruth M. Wunderlich. *Jour. Ind. Hyg.*, July, 1921, pages 79-92, and August, 1921, pages 137-146.

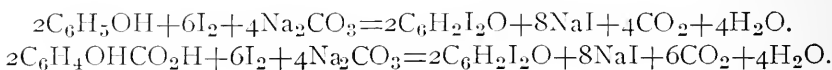
I—Carbon monoxide is the only considerable toxic substance in the exhaust gas from gasoline. From benzol and illuminating gas, accessory poisonous substances result in the exhaust.

II—A concentration of 15 parts of carbon monoxide per 10,000 parts of air is dangerous to life.

III—If a car while "warming up" should give off 1 cubic foot of carbon monoxide per minute in a closed room 10 by 10 by 20 feet, the atmosphere would reach the dangerous concentration of 15 parts per 10,000 in three minutes, R. P. F.—(Abstracted from *Pub. Health Reports*, United States Public Health Service, Vol. 36, No. 36, Sept. 9, 1921.)

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ESTIMATION OF SALICYLATES AND PHENOL.—In a method proposed for the estimation of these compounds advantage is taken of the characteristic behavior of the constituents phenol and salicylic acid towards iodine; the final product of the reaction in the presence of alkali or alkaline carbonate is a purplish-red amorphous compound  $C_6H_2I_2O$ , termed diiodophenylene oxide or tetraiodophenylene quinone. The reaction is represented by the equations:



Each molecule of phenol, salicylic, or acetylsalicylic acid yields one molecule of the iodine compound, whilst one molecule of salol yields two molecules of the same compound. In the case of salol, about 0.1 gm. of the sample is weighed on to a small dry filter and washed with successive quantities of chloroform until all soluble substances have been dissolved; the chloroform solution is evaporated at the ordinary temperature in a conical flask, the dry residue obtained is treated with 10 cc. of a 1 per cent. sodium hydroxide solution, and the mixture heated under a reflux apparatus so that boiling begins in about two minutes. Successive quantities of 10, 30, and 50 cc. of water are then added, the heating being so regulated that the mixture begins to boil in about 3, 5, and 10 minute intervals respectively. Just before the last addition of water, 1 gm. of dry sodium carbonate is introduced into the top of the condenser and washed down with the water. To the clear boiling solution is now added 60 cc. (or an excess) of N/5 iodine solution, the mixture again boiled, the condenser then rinsed with a small quantity



of water, and the flask disconnected. A further 1 gm. of sodium carbonate is added, and the mixture boiled gently for 20 minutes; care must be taken during this period, as the evolution of carbon dioxide causes much frothing. The precipitate is then collected on a weighed filter, washed with not less than 200 cc. of hot water, dried at 100° C. and weighed. The weight found is multiplied by 0.3113 to obtain the amount of salol present. Acetanilide, phenacetin, and caffeine do not interfere with the estimation, but when phenacetin is known to be present, the quantity of iodine should be increased by 5 cc. for each 0.1 gm. of phenacetin. With a mixture of salol and acetanilide, the filtrate from the precipitate is practically colorless; but when phenacetin is present the filtrate is colored light yellow, so that it is not easy to recognize whether or not an excess of iodine is present.—Emery (*J. Ind. Eng. Chem.*, 1921, pp. 538-539, through *Analyst*, 1921, p. 376).

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ESTIMATION OF LECITHIN.—In Hager's method of estimation the lecithin is decomposed by boiling with nitric and sulphuric acids, and the phosphoric acid precipitated with ammonium molybdate. The precipitate is washed, suspended in water, and dissolved in semi-normal alkali hydroxide solution, an excess of 5 to 6 cc. being added, and the solution boiled until all ammonia is expelled, and then titrated with semi-normal hydrochloric acid. Each cubic centimetre of decinormal alkali corresponds (according to Hager) with 1.268 mgm. of  $P_2O_5$ . The author finds this method tedious and quite unreliable. The phosphoric acid may be estimated directly in the residue obtained after removal of organic matter by a mixture of nitric sulphuric acids. The acid is first neutralized with alkali, and ammonium chloride and ammonia are added until a precipitate forms, which is then dissolved in dilute hydrochloric acid. Magnesia mixture is added, and the solution is treated with ammonia at boiling temperature. It is not possible, however, to determine the amount of lecithin in a sample from its  $P_2O_5$  content, as the formula  $C_{42}H_{84}NPO_9$  is doubtful.—(J. L. B. VAN DER MARCK, *Pharm. Weekblad.*, 1921, 989-992, through *Chem. and Drugg.*)

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FAT-SOLUBLE VITAMIN AND YELLOW PIGMENTATION IN ANIMAL FATS.—There is a very high concentration of the fat-soluble vitamin in cod liver oil, but only small amounts of yellow pigments.

Butter fat shows a seasonal variation in the fat-soluble vitamin content when obtained from stall-fed cows during the winter and pastured in the summer. The fat-soluble vitamin content of butter fat does not run closely parallel to the yellow pigment; yet, in general, due to determination by their content in the feed, butters highly pigmented are rich in the vitamin; butters low in pigment should be looked upon with suspicion. In beef fats the relations are somewhat similar; those most pigmented are also generally richest in their fat-soluble vitamin content. The fat-soluble vitamin withstands severe methods of saponification. This indicates that it is not a fat, and probably not an ester.—(H. STEENBOCK, M. SELL and M. V. BUELL, [*Journ. Biolog. Chem.*, Baltimore, June, 1921, p. 89; through *Journ. Amer. Med. Assoc.*, July 9, 1921, p. 152.] )

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INSECT POWDER DERMATITIS.—An occupational dermatitis has been found to occur among the workers engaged in the manufacture of pyrethrum insect powder. Chemical analyses of pyrethrum have established various constituents having irritant properties. The lesions noted are, essentially, various forms of dermatitis venenata. They are of mild severity and quickly disappear under ordinary treatment. Re-exposure frequently leads to the reoccurrence of the disease. This dermatitis may be prevented by the introduction of trade processes that eliminate the necessity of exposure of workers to pyrethrum dust and powder.—(Through *Journ. Amer. Med. Assoc.*)

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EFFECT OF COLD AND FREEZING ON CERTAIN PREPARATIONS.—E've has studied the effect of freezing upon magnesium magma and finds that after freezing and thawing the normal water content of the magnesium hydroxide gel is changed, with the result that molecules of magnesium hydroxide unite to form a fine crystallized powder. This formation is practically irreversible and cannot be brought back to the colloidal state. Other pharmaceutical preparations are likewise affected by freezing; Magma of bismuth subcarbonate, elixirs containing terpinol hydrate, Fowler's solution, compound solution of sodium phosphate, compound solution of hypophosphites, and solution of hydriodic acid, solution of ferrous iodide, and solution of hydrogen peroxide.—(*Amer. Druggist.*)

A NEW ANTIFEBRILE FROM INDIA.—Investigations are being made at present into the medicinal properties of a forest tree indigenous to parts of Bihar and Bengal that recall the circumstances under which quinine became known to the world as a remedy for malarial fever. The late civil surgeon of Ranchi, Lieut. Col. J. C. S. Vaughan, having noticed the occurrence of a large number of cases of malignant malaria and blackwater fever in that district, made inquiries among the aboriginal tribes to find whether they used any local plants as a cure for these diseases. It appears that there is a tree whose leaves, bark, and root are all used, and experiments that have been made with the leaves raise the hope that they may prove to be a valuable addition to our stock of drugs for use in the Tropics.

The tree is known by various vernacular names, but its botanical name is *Vitex peduncularis*. It is found not only in Chota Nagpur but also in eastern Bengal and the Khasia Terai. The simplest way to use it is to make an infusion of the leaves—1 ounce of leaves to 40 ounces of infusion. The effect has been found to vary, but this is true of quinine as well, and of most other drugs. In most cases larger doses or stronger infusions proved effective where the ordinary treatment had failed, and microscopic examination proved that the malarial parasites disappeared from the blood under the influence of the treatment. As these results have been obtained by using the drug in its crudest state, it is hoped that in concentrated form it may prove even more satisfactory. It has advantages over quinine in having no bitter taste or toxic properties, of being a stimulant rather than a depressant, and of being suitable for children and for people in delicate health. It is said to have been useful in influenza, and in cases of blackwater fever it has given very good results.—(Through *Commerce Reports*, June, 1921.)

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SWEETENING AGENTS; DEFINITIONS AND UNITS IN CHEMISTRY OF—. T. Paul. *Chem-Zeit.*, 1921, 45, 705-706.—The "degree of sweetness," SG (*Süssungsgrad*), of a substance is defined as the number of g. of pure sucrose which, in a given volume of water, has the same sweetening effect as 1 g. of the substance. The degree of sweetness of dextrose was found to be 0.52, that of levulose 1.03, lactose 0.28, mannitol 0.42, and that of a starch syrup containing 78 per cent. of solids 0.26; these values appear to be inde-

pendent of the concentration, at least for sucrose concentrations between 20 and 100 g. per l. For saccharin and dulcin, SG diminishes with increasing concentration, the values corresponding to sucrose concentrations of 20, 60, and 100 g. per l. being 667, 316, and 187 in the case of saccharin, and 364, 90, and 70 respectively in the case of dulcin. The degree of sweetness of a mixture of saccharin and dulcin is greater than that calculated from the values for the ingredients; *e. g.*, 280 mg. of saccharin and 129 mg. of dulcin, in a litre of water, have the same sweetness as 535 mg. of saccharin alone in the same volume. The "sweetening unit," SE (*Süssungseinheit*), of a substance is defined as the number of g. required to produce the same effect as 1 kg. of sucrose, in a given volume of water.—(J. H. L.; through *The Analyst*.)

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GLYCEROPHOSPHATES; DETERMINATION OF SMALL QUANTITIES OF PHOSPHATES IN —. J. L. Lizius. Brit. Pharm. Conf., June, 1921. *Pharm. J.*, 1921, 106, 478-479.—One gm. of the glycerophosphates is dissolved in 50 cc. of water and the solution is added from a burette to a mixture of 10 cc. of 25 per cent. nitric acid and 10 cc. of 10 per cent. ammonium molybdate solution until the coloration obtained is equal to that produced by a known amount (*e. g.*, 0.0002), of phosphoric acid in the same amounts of reagents. If 10 cc. of the glycerophosphate solution is required, the sample will contain 0.1 per cent. of phosphoric acid in inorganic combination. To apply the method to ferric glycerophosphate, the sample is dissolved in dilute nitric acid, heated, treated with sodium hydroxide, the ferric hydroxide separated by filtration, the filtrate diluted to 50 cc. and used for the determination.—(W. P. S.; through *The Analyst*.)

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VANILLA EXTRACTS; DETERMINATION OF THE LEAD NUMBER OF —. H. J. Wichmann. *J. Ind. Eng. Chem.*, 1912, 13, 414-418.—The following procedure is recommended to obtain a maximum precipitation and to combine determinations of the lead value and alcohol content of vanilla extracts. A mixture of water, 175, 8 per cent. normal lead acetate solution, 25 and vanilla extract, 50 cc. is distilled; 200 cc. of distillate is collected and the alcohol content is calculated from the sp. gr. of the distillate. The residue in the distillation flask is diluted to 100 cc. with water free from carbon

dioxide, filtered, and 10 cc. of the filtrate is mixed with 25 cc. of water, 10 cc. of dilute sulphuric acid and 100 cc. of alcohol are added; the precipitated lead sulphate is collected and weighed. A control determination is made at the same time, using water containing 5 drops of glacial acetic acid in place of the vanilla extract. The quantity of lead precipitated by the extract and expressed as g. per 100 cc. is the lead value; for genuine undiluted extracts it is not less than 0.55. Sugar, glycerol, and coumarin do not interfere with the determination; if added vanillin is present it must be removed by extracting 50 cc. of the sample with three successive quantities of 50 cc. of a mixture of equal vols. of ether and petroleum spirit; the extracted aqueous solution is then used for the determination.—(W. P. S.; through *The Analyst*.)

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ALCOHOL AS LOCOMOTIVE FUEL IN BRAZIL.—Consul C. R. Cameron of Pernambuco, reports that there are in his district approximately eighty modern cane-sugar factories, which have about 800 miles of railway, of from 0.75 to 1 meter gauge, operated at present by wood-burning locomotives. The fuel problem, however, is becoming a serious one and as a result the sugar-mill operators are turning their attention to the matter of reducing wood consumption and the substitutes. Consequently great interest is being shown in the substitution of alcohol, which is produced in large quantities on the sugar plantations from the molasses finals. Pernambuco has recently adopted the use of alcohol to which 5 per cent. gasoline has been added as an automobile fuel (see *Commerce Reports*, Mar. 15, 1921). The manufacturers are, therefore, naturally interested in using their own inexpensive product for their railways. The current price of alcohol is about \$0.22 per gallon, but the cost to the producer is much less. It is suggested that American manufacturers of locomotives capable of burning alcohol communicate with the Pernambuco sugar mills, a list of which may be obtained from the Latin-American Division of the Bureau of Foreign and Domestic Commerce or from any of the district or co-operative offices by referring to File No. L. A. 12012.—(Through *Commerce Reports*.)

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FORMALDEHYDE AND PARA-FORMALDEHYDE; DETERMINATION OF  
—IN TABLETS. N. Evers and C. M. Caines. Brit. Pharm. Conf.,  
June, 1921. *Pharm. J.*, 1921, 470.—A tablet is weighed, boiled with

200 cc. of water for 30 mins. under a reflux condenser, the solution cooled, diluted to 500 cc. and filtered. Ten cc. of the filtrate is placed in a test-tube and a series of standards is prepared in 10 test-tubes, these containing, respectively, quantities of 0.1 to 1.0 cc. of 0.0038 per cent. formaldehyde solution, and each diluted to a volume of 10 cc. To each tube is added 2 cc. of Schiff's reagent and the colorations obtained are compared after the lapse of 3 mins. The presence of lactose, sucrose, and menthol does not interfere.—(W. P. S.; through *The Analyst*.)

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ESTIMATION OF SANTONIN IN WORMSEED.—Kariyone and Kimura recommend the following method for the assay of wormseed: 10 gm. of powdered wormseed is extracted with ether for three hours in a Soxhlet extractor. The ether is removed by evaporation, and the residue boiled for thirty minutes, under a reflux condenser, with 100 cc. of barium hydroxide solution (5 per cent.). The solution, after being saturated with carbon dioxide until it turns blue litmus red, is then filtered. Eighty cc. of the filtrate (=8 gm. of drug) is placed in a separator of 200 cc. capacity; 10 cc. of hydrochloric acid (15 per cent.) and 20 cc. of chloroform are added, and the mixture is vigorously shaken for two minutes. After standing for a few minutes the clear chloroformic solution is filtered through a filter, previously moistened with chloroform, into a flask of 200 cc. capacity. The acid solution is then shaken three times, using on each occasion 10 cc. of chloroform, each washing being filtered through the same filter. The total chloroformic solution is evaporated to dryness, and the residue dissolved in 30 cc. of hot alcohol. After cooling, the alcoholic solution is neutralized with N/10 solution of potassium hydroxide, using phenolphthalein as indicator. Thereupon 20 cc. of N/10 solution of potassium hydroxide is further added, and the mixture boiled for thirty minutes under a reflux condenser. After cooling, it is re-titrated with N/10 hydrochloric acid. On the other hand, 30 cc. of the alcohol used to dissolve the chloroformic extract is treated with 20 cc. of N/10 solution of potassium hydroxide in the same way as described above, and neutralized with N/10 hydrochloric acid. If the number of cc. of N/10 hydrochloric acid used in the first instance is =X, and in the second test =Y, the percentage of santonin present is calculated by the use of the following formula:

$$\text{Percentage of santonin} = \frac{(Y-N) \times 2.462}{8}$$

This method was found to be superior to that of Katz, particularly in the presence of small amounts of santonin.—(Through *The Pharm. Jour. and Pharm.*)

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ISO-ALCOHOLIC ELIXIR.—With the object of using a minimum amount of alcohol so as to produce an elixir of an alcoholic strength, just sufficient to dissolve the medicament of which it is the vehicle, Dr. Bernard Fantus and Mr. C. M. Snow have devised the following formula:

Compound spirit of orange .....	10
Syrup .....	375
Purified talc .....	30
Alcohol .....	50
Glycerin .....	200
Distilled water to make .....	1,000

Mix the compound spirit of orange with the alcohol. Add the glycerin, syrup, and then the water, each of these in several portions, agitating after each addition. Mix the purified talc intimately with the liquid, and then filter through a wetted filter, returning the first portion of the filtrate until a transparent liquid is obtained.

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## NEWS ITEMS AND PERSONAL NOTES

SCIENTIFIC BODY HONORS PHARMACIST EXPLORER.—The American Pharmaceutical Association assembled for its annual meeting at New Orleans has shown its respect and high esteem for one of its leading members, Dr. Henry H. Rusby, Dean of the College of Pharmacy, Columbia University. Doctor Rusby is now in the interior of Bolivia, La Paz, directing the work of the Mulford Exploration. His object is the search for new drugs and medicinal plants together with botanical and zoological specimens of all kinds.

Doctor Rusby is no longer a young man and his boldness in undertaking a tropical exploration of this kind is hailed by his friends as one of the heroic phases of modern pharmaceutical and botanical science.

By unanimous vote the following message was cabled to Doctor Rusby:

"The American Pharmaceutical Association in convention assembled at New Orleans September 8, 1921, sends hearty greetings to Prof. Henry H. Rusby, and wishes him a successful consummation on his exploration trip and a safe return therefrom."

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AMBROSE HUNSBERGER, THE NEW PRESIDENT OF THE N. A. R. D.—The good wishes of this Journal are herewith conveyed to the new president of the National Association of Retail Druggists. A real pharmacist, ever interested in the welfare of his profession and willing to work in its interest, Mr. Hunsberger well deserves this additional honor which has come to him. The Association which has so honored him is to be congratulated upon engaging the services of so valuable and constructive a leader.

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MERCK'S NEW REAGENT CATALOG AND PRICE LIST.—Merck & Co. are distributing a new edition of their booklet *Blue Label Reagents and Other Laboratory Chemicals*. Merck's Blue Label Reagents, familiarly known as M. B. L., are made according to the requirements in *Standards and Tests for Reagent Chemicals*, published in 1920 by D. Van Nostrand & Co., of New York, and a special feature of the new catalog is the concise summary under each reagent showing its standard of purity, methods of testing, and other data taken from that textbook with the author's permission. Such of Merck's "White Label" chemicals of H. P., "C. P.," and other grades as are of particular interest to laboratory workers are also listed and current prices are given throughout. The booklet, therefore, should be of interest to chemists generally as a manual and price list.

Copies may be obtained by addressing Merck & Co., 45 Park Place, New York.

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PENNSYLVANIA STATE MEDICAL SOCIETY MEETING.—One of the features of the Pennsylvania State Medical Society meeting, held in Philadelphia during the week of October 3, was a visitation to the Mulford Biological Laboratories, at Glenolden, Pa., which is just nine miles outside of the city.



A large number of the members, with their wives and friends, took advantage of this opportunity to view the largest biological laboratories in this country, if not in the world, to see how anti-toxins, vaccines, serobacterins, etc., are made, and to see many of the actual operations, such as injecting and bleeding of horses, etc.

Special trains had been provided by the H. K. Mulford Company for conveying the visitors to and from the laboratories. Refreshments were served on the grounds, and there was a barn dance for the amusement of those who were not particularly interested in the scientific work.

A feature which attracted special attention was the parade of immunized horses, in which these handsome and noble beasts passed proudly in review, as though conscious of the great service they are rendering to humanity.

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## BOOK REVIEWS

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OSMOTISCHE UNTERSUCHUNGEN. Studien zur Zellmechanik von Dr. W. Pfeffer. Second, unchanged edition, with five woodcuts. Leipzig, William Englemann.

Dr. Pfeffer was Professor of Botany in Basel when he undertook a series of investigations into the phenomena of osmosis, the results of which proved one of the most important phases in the development of physical chemistry. The volume in hand is a reprint of his work, published in 1876, issued as a memorial of the author, who died in January, 1920. The history of the subject shows, as usual in science, a very early anticipation of the general features of the investigation, Pfeffer giving in his book a summary of the data. As early as 1748, the Abbé Nollet noted osmotic action, but his work attracted so little attention that a later investigator, Fischer, was considered by many as the discoverer. In the second quarter of the nineteenth century, Dutrochet made investigations and introduced the terms "endosmose" and "exosmose" for the respective movements of currents in and out of the cell. As far as nationalistic feelings are concerned, the honors appear, indeed, to be fairly easy; the names of Pfeffer, Dutrochet and Graham being about equally prominent in the early history. Graham's early results in

1854 were of great importance, leading to the introduction of the terms "crystalloid" and "colloid" and to the process of dialysis. "Colloid chemistry" has become a most important branch of the science.

It is interesting to note that Pfeffer was a botanist, and that his studies were determined by his interest in the physiology of the living cell. It was Pfeffer who made the ingenious improvement by which the membrane was able to sustain a high pressure. The highest osmotic pressure will be obtained when the membrane is permeable by the dissolving medium (solvent) and not by the dissolved substance (solute). Pfeffer employed a porous cup in the walls of which copper ferrocyanide was produced by the diffusion of copper sulphate and potassium ferrocyanide from opposite sides. This pot was connected with a manometer tube. Naturally, this early apparatus was not entirely satisfactory, and improvements have been made so to secure greater accuracy, yet Pfeffer's results remained for a long time the principal data, being indeed, the only quantitative measurements, and produced a deep effect on the history of the chemistry and physics of solutions.

The publisher presents in the present volume, as already noted, an exact reprint of the original work, which appeared in 1876, except addition of a note by Dr. F. Czapek. Reference is made in this introduction to the important additions to the knowledge of the physical chemistry of solution by H. N. Morse and his co-workers in the laboratory of the Johns Hopkins University. An account of these investigations appeared in pamphlet form in 1914, under the title of "The Osmotic Pressure of Aqueous Solutions." The extensive studies since made in this field are familiar to physical chemists.

The book itself is well printed and is an interesting contribution to the classics of chemistry. Physical chemical phenomena received but scant notice in the manuals of physics or chemistry in the days when Dutrochet, Graham, Pfeffer and many others were working, and the topic first made its appearance in manual of chemistry as "chemical physics," but now it forms the subject of independent manuals and has a large part in the literature of the science.

The firm of Wilhelm Englemann deserves the thanks of chemists for re-issuing this important and interesting contribution, the

original addition having been long out of print. The price of the book is given as 32 marks, bound, with the usual note of high percentage increase under the rulings of the trade union, but in view of the changing value of the mark the price to the American buyer is uncertain.

HENRY LEFFMAN.

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A TEXTBOOK OF ORGANIC CHEMISTRY. By JOSEPH S. CHAMBERLAIN, Ph. D., Professor of Organic Chemistry, Massachusetts Agricultural College. P. Blakiston's Sons and Company, Philadelphia. \$4 net.

This work of 927 pages is an attempt on the part of the author "to present the subject (of organic chemistry) in a sufficiently elementary manner so as not to be beyond the grasp of the student in his first course in organic chemistry, yet, at the same time to make the book comprehensive in that it takes up the entire field by taking up practically all of the important groups of compounds." "The book is written primarily as a textbook for the undergraduate student and the instructor," but, in the opinion of the reviewer, the author has reason for his hope "that those who have already studied the subject may find it of value for its general presentation."

It is written in more or less of free lecture style, in language that is easily understood. There is some repetition of steps involved in reactions but all is to the advantage of the reader. In this sense it may be considered elementary, but when one notes the very large number of classes of compounds and individual compounds that are mentioned he must admit that in this sense the book is far from elementary.

A careful reading of the most of the text discloses but very few errors, something which cannot be said truthfully of many new works. Paper and typography are good. In addition to 31 pages, in double column, of index, there are 35 pages devoted to a survey of contents.

The reviewer knows of no recent book which he would more earnestly recommend to students in schools, and others who wish a good general survey of the field of organic chemistry.

F. P. S.

ORGANIC COMPOUNDS OF MERCURY. By FRANK C. WHITMORE, Ph.D. 397 pages. The Chemical Catalogue Company, Inc., New York. Price, \$4.50.

This book is the third of a series of monographs to be issued by the American Chemical Society on subjects of current interest, written by persons who are considered authorities on their respective subjects. The purpose of these monographs is to present the available knowledge on the chosen subject in readable form and to promote research in the branch of science concerned in each particular subject.

This particular book is claimed to be the only one in any language on this subject. Not all organic compounds which contain mercury are considered, the book treating almost solely of the true organic compounds of mercury in which the element is attached directly to carbon. Compounds of mercury not discussed in the text are made available for study by the supplementary bibliographical lists in the Appendix.

The arrangement of compounds is such as serves the general chemist who wishes to know what has been done in the field as a whole, as well as the specialist who wishes to learn quickly what has been done in any particular portion of the field.

The subject matter is divided into fourteen chapters covering 345 pages, and treats of General Methods of Preparation and General Properties and Reactions of Organic Mercury Compounds, and Mercury Derivatives of the various classes of Organic Compounds.

Five appendices take up Analysis of Organic Mercury Compounds, List of Proprietary Mercurials, an extensive Bibliography of Biological and Pharmacological Work with Organic Mercury Compounds, List of Patents dealing with Organic Mercury Compounds. Finally, there is a good subject index as well as an author index.

F. P. S.

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## EDITORIAL

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### BARIUM SULPHATE.

Of recent years this chemical has come into considerable use. Its particular field of usefulness has been in röntgenological practice. Previous to its introduction the bismuth compounds had been used to supply imperviousness to the passage of the X-ray so that organs coated with the chemical reflected their outlines or defects in their outlines on the developed negatives. But the bismuth compounds were expensive, and minds were promptly turned to search for some innocuous and inexpensive substitute to replace these costly compounds. Of the host of substances which presented themselves, barium sulphate was selected and under some conditions proved to be quite the happy choice. It is, however, painfully true that deplorable errors have been made in many instances in connection with dispensing this substance. A recent fatal mistake is reported in the English press, which recounts how barium thiosulphate, also known as barium hypo-sulphite, had been administered instead of the sulphate, and had occasioned the prompt death of the patient to whom it had been furnished. (See *Pharmaceutical Journal and Pharmacist*, October 22, 1921.)

On this side of the water barium sulphide, the depilatory, has often been given in error for the insoluble sulphate, and frequently with fatal results. All of these mistakes have occurred when the chemical in question had been prescribed for the purpose of affording X-ray diagnosis. Those who are familiar with procedures involving the use of these impervious materials for röntgenology know that the custom is to administer to the patient a quantity of the chemical ranging from 100 to 150 grammes suspended in water or preferably milk. Then, after the customary delay, the exposure is

made and the impervious material is allowed to follow the usual course of passage through the body canals. It naturally follows that only an insoluble and innocuous compound can be safely used for this purpose because of the enormity of the bulk dose and also because of leaving the material in the digestive organs until it is disposed of by natural processes. Pure barium sulphate is practically insoluble in water and in dilute acids, and from that viewpoint can be used with impunity for the stated purpose. Pure barium sulphate is easily procurable from the responsible chemical manufacturers if the purchaser is satisfied to pay a slightly increased price, but there is much of this material placed upon the market today and offered at lower figures than the pure compound which is totally unfit for this diagnostic purpose.

Knowing the comparative toxicity of the soluble compounds of barium and also knowing that variable and unscientific modes of manufacturing this chemical might by occlusion or otherwise contaminate the precipitated sulphate with soluble compounds of barium or other bases, the need for watchfulness and eternal care in using suspicious samples is very manifest.

We have recently encountered samples of the so-called X-ray barium sulphate that emitted the familiar odor of hydrogen sulphide, and we recall one instance where a hospital laboratory submitted to us a compound, the manufacturing source of which was not specified, that was possessive of this odor to an unusual extent. This particular sample carried with it the reputation of having caused much discomfort to a series of patients to whom it had been administered and a good deal more discomfort to the roentgenologist who had used it. A cursory examination of it revealed the presence in the dried material of about three-tenths of one per cent. of water soluble residue, which was composed in the main of calcium sulphate and of sulphides of zinc and calcium, impurities which were probably due to the manufacturing process. Assuming that one-half of this residue consisted of the sulphides of zinc and calcium, one can readily see that a patient to whom is administered 150 grammes of the compound receives of these sulphides a unit dose approximating .275 gramme, or about 4 grains, a dose which, while not toxic, is at least nauseating.

The sulphides of barium, were they present in a like proportion would certainly lead to more serious results, but it is hardly

likely that these compounds are present from manufacturing defects. It has been said, however, that long storage of the barium sulphate under some conditions would lead to a reduction of some of the sulphate into the sulphides. That in the presence of dampness and organic contaminants certain bacterial agents are able to reduce small amounts of the sulphate to the several sulphides is the opinion of a scientist who was consulted with in this matter. Another propounded the theory that moisture alone could effect changes in the composition of this chemical.

Summing up, these facts remain clear. In the first place that as long as this chemical is not included in the present revision of the United States Pharmacopœia so that adequate protective tests might be consulted and used, those utilizing this as their impervious agent should be particularly meticulous in regard to its source, its purity and its storage. In the second place, the product of reputable manufacturers should be specified and along with these specifications should be added the designation upon the order sheet, "Barium Sulphate, Pure, for X-ray purposes." Any samples giving an odor of the sulphides should be viewed with suspicion and should not be administered to patients, except after previously thoroughly washing in dilute acid and water. Also this material should never be stored except in dry containers and in a dry place.

I. G.

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## ORIGINAL PAPERS

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### LACTOMETER AND FAT IN MILK CONTROL.\*

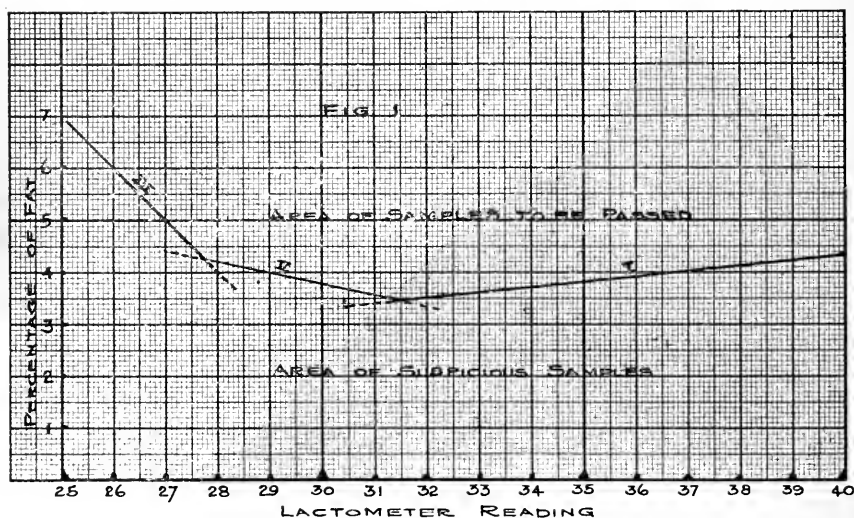
By DAVID WILBUR HORN, Ph. D.

This paper calls attention to a method for using jointly the lactometer reading and the butter-fat content of a milk directly as the bases for sorting out skimmed, watered, and sub-standard milks. This method is for preliminary use in routine examinations of so-called *herd milks* or *market milks*. It is logical that the lactometer reading and the percentage of fat should serve directly to guide the

\*Read before the Delaware County Institute of Science, Media, Pa., May 9, 1921.

later detailed work because these are the values determined at the outset in routine milk work.

In States that, like Pennsylvania, have expressed in the statutes<sup>1</sup> minimum legal percentages of fat and total solids, and that do not provide additional penalties for skimming and watering,<sup>2</sup> the analyst does well to confine his evidence to data showing the milk in question to be sub-standard. It is worth while in such States to establish that a suspected milk is skimmed or watered only in those cases where the percentages of fat and of total solids are



above the legal minima. The method suggested in this paper embodies this idea.

In normal mixed milks the constituents are present in fairly constant proportions. The relations between various constituents have found expression in numerous *milk formulæ*<sup>3</sup> some of which

<sup>1</sup> Milk and Cream Act, approved June 8, 1911, forbids the sale of "milk which contains less than three and one-quarter ( $3\frac{1}{4}$ ) per centum of butter-fat, and less than twelve (12) per centum of milk solids," etc.

<sup>2</sup> In the State of Massachusetts, the penalty for the sale of milk which is adulterated is more severe than for the sale of milk below the legal standard." Lythgoe, *Jour. Ind. Eng. Chem.*, VI, p. 900, 1914. See also, *Journ. Off. Agr. Chemists*, August, 1921.

<sup>3</sup> These may be found in various text-books. Among the more valuable of the recent formulæ are those due to Lythgoe (footnote 2) resting upon the total solids, the sugar, the fat and the ash, which may be used in distinguishing



are so generally used that instead of the analyst going to the formulæ themselves or to a table of values derived from them, slide rules are available for the necessary calculations.<sup>4</sup> Some of the milk formulæ that are most extensively used date back thirty to thirty-five years and have survived the scrutiny of critics and the proof of practice. Two formulæ of which this may be said are (1) the formula<sup>5</sup> connecting the percentage of total solids T with the lactometer reading L and the percentage of fat F:

$$T = \frac{1}{4}L + \frac{1}{2}F = 0.25L + 1.2F \dots\dots\dots (1)$$

and (2) the formula<sup>6</sup> connecting the mean specific gravity of the total solid matter *m* with the specific gravity of the milk *G* and the percentage of total solids T contained in it. The removal of fat or the addition of skimmed milk raises this mean specific gravity; the first, because it removes some solids that are lighter than water, the second, because it increases the proportion of solids that are heavier than water. The relation between this mean specific gravity of the solids and the other values in a milk can be and has been clearly demonstrated to be quantitative.<sup>7</sup> This relation has

between pure and adulterated milk. As in the early use of most milk formulæ, "subsequent experiences (between 1909 and 1914) showed that "for practical purposes" certain changes were desirable in the application of them.

<sup>4</sup>Richmond's "Milk Scale" and Ackermann's "Automatic Reckoner."

<sup>5</sup>This simple form is often called Richmond's, or Richmond and Hehner, or Babcock's formulæ. As a matter of fact it is a simpler form of expression that became apparent when more complicated formulæ were applied and the tabulated results then compared. See Richmond's *Dairy Chemistry*, 2d Ed., 1914, p. 69; and Shaw and Eckles, Bull. 134, U. S. Dept. Agr., Bur. of Animal Ind., 1911. Richmond and Hehner's formulæ (*Analyst*, 13, p. 26, 1888),  $T = 0.254 G + 1.164 F$ , which approximates closely to  $T = \frac{1}{4} G + \frac{1}{2} F$  Richmond later derived a new formula because the previous formulæ "were derived from analyses to which objection could be taken"; so that Richmond's

formula is  $T = 0.2625 \frac{T}{G} + 1.2 F$ , which has been found to be expressed by

the simpler formula,  $T = \frac{G}{4} + \frac{6}{5} F + .14$ ; and this is the formula on which

Richmond's milk scale rests. In this country it is customary to drop the constant, as suggested by Patrick (see Leffman, *Analysis of Milk and Milk Products* 1915, p. 21); and after so doing, the formula is frequently called Babcock's formula. Babcock's papers are in the 8th and 12th Ann. Rep. Wisconsin Agr. Exp. Sta., 1891 and 1895. See Allen's *Com. Org. Anal.*, 4th Ed., Vol. VIII, p. 163.

<sup>6</sup>Known as Fleischmann's formula, which dates back in its beginnings to 1882-85 (*Jour. für Landwirtschaft*, 30, p. 293; 33, p. 251.).

<sup>7</sup>For demonstration, see Richmond's *Dairy Chemistry*, p. 64.

been thus expressed:

$$m = \frac{GT}{GT - (100G - 100)} \dots\dots\dots (2)$$

The numerical value of  $m$  ranges from 1.2 to 1.4, depending upon the ratio obtaining in any given milk between the fat and the non-fatty solids. It does not exceed 1.34 in mixed milks beyond suspicion of skimming.<sup>8</sup> If therefore the value 1.34 be substituted for  $m$  in equation (2), thus,

$$1.34 = \frac{GT}{GT - (100G - 100)} \dots\dots\dots (3)$$

an equation (3) is obtained that defines the minimum values of  $G$  and  $T$  that will be met with in mixed milks which may in routine examinations be passed as unskimmed.

Formulae that serve to bring out probable skimming are more generally useful in routine work than other milk formulae. The writer's experience leads to the conclusion that in 1920 in the suburban area from which the market milk samples (upward of a thousand) examined by him were drawn, skimmed milk was from thirty to forty times as common as watered milk or as sub-standard milk. This is largely due to the fact that the larger dealers practice skimming in one form or another under the name *standardization*.<sup>9</sup> Therefore the first and most important step in developing the sorting method herein proposed was to obtain a formula involving only the lactometer reading  $L$  and the fat per cent.  $F$ , by which milks suspicious of skimming would be indicated.

Such an equation was developed algebraically from (1) and (3). In the development it is necessary to make use of the fact that the lactometer reading  $L$ , expressed as it usually is in degrees on the Quevenne lactometer scale, bears the following relation to the specific gravity  $G$  of the milk (provided both readings are at the standard temperature, 60° F.):

$$L = 1000G - 1000. \dots\dots\dots (4)$$

whence,

$$G = \frac{L + 1000}{1000} \dots\dots\dots (5)$$

<sup>8</sup> See Van Slyke, *Modern Methods of Testing Milk and Milk Products*, 1907, p. 140; and Woodman, *Food Analysis*, 1915, p. 139.

<sup>9</sup> See Parker, *City Milk Supply*, 1917, p. 261.

Transforming equation (3), it may be made to assume the form,

$$T = \frac{3.941 (100 G - 100)}{G} \dots\dots\dots (6)$$

Substituting into (6) the value for G from (5), equation (3) finally may be made to assume the form,

$$T = \frac{394.1 L}{L + 1000} \dots\dots\dots (7)$$

Equating the values for T as given in (1) and (7), one obtains

$$\frac{394.1 L}{L + 1000} = 0.25 L + 1.2 F \dots\dots\dots (8)$$

which reduces to

$$F = \frac{328.42 L}{L + 1000} - 0.2083 L \dots\dots\dots (9)$$

This formula meets the requirements of the case since it involves only the lactometer reading L and the fat per cent. F, and by it mixed milks suspicious of skimming will be indicated.

Another formula that the writer has used as a check upon the numerical results from (9), was developed by substituting the value for L as given in (4) into equation (1) and then equating the right hand member of the resulting equation, which is.

$$T = \frac{5 (100 G - 100)}{2} + \frac{6}{5} F \dots\dots\dots (10)$$

with the right hand member of equation (6). After simplifying one then obtains the formula

$$F = \left( \frac{3.284}{G} - 2.083 \right) (100 G - 100) \dots\dots\dots (11)$$

The numerical results calculated by each of these formulæ are given in the following table. The values found thus for F have been rounded off so that they might not exhibit fictitious accuracy.<sup>10</sup>

<sup>10</sup> "The fat calculated from the specific gravity and total solids almost invariably agrees within 0.2 per cent. with the determination made by the appropriate method." Richmond, *Dairy Chem.*, p. 69.

TABLE I.

<i>Specific gravity at 60° F.</i>	<i>Lactometer reading at 60° F.</i>	<i>% fat calculated by formula (9)</i>	<i>% fat calculated by formula (11)</i>
1.025	25	2.8	2.8
1.026	26	2.9	2.9
1.027	27	3.0	3.0
1.028	28	3.1	3.1
1.029	29	3.2	3.2
1.030	30	3.3	3.3
1.031	31	3.4	3.4
1.032	32	3.5	3.5
1.033	33	3.6	3.6
1.034	34	3.7	3.7
1.035	35	3.8	3.8
1.036	36	3.9	3.9
1.037	37	4.0	4.0
1.038	38	4.1	4.1
1.039	39	4.2	4.2
1.040	40	4.3	4.3

Upon inspection of this table, a surprisingly simple relation between the lactometer reading and the fat per cent. becomes evident. The numerical values for the fat may be obtained by adding 3 to the lactometer reading and then dividing by 10. This is expressed by a much simpler formula than either of those originally used to calculate the values of *F* set forth in Table I:

$$F = \frac{L + 3}{10} \dots\dots\dots (12)$$

From the derivation of formulæ (9) and (11), and hence of this simple formula (12), it follows that any one of the fat values calculated by formula (12) is the lowest or minimum fat percentage to be expected in an unskimmed mixed milk that has exhibited the corresponding lactometer reading. As an example of the use of this formula, consider a mixed milk found to have a lactometer reading of 32; the minimum fat per cent. in such a milk if it is above suspicion of skimming is

$$(32 + 3) \div 10 = 3.5\%.$$

Should the milk be found by actual analysis to contain less than 3.5 per cent. it should be set aside for further consideration because it is not above suspicion of being skimmed.

A rule so simple is easily remembered, and applied without written calculations: *Add 3 to the lactometer reading and then divide by 10. The result is the minimum percentage of fat in a mixed milk above suspicion of being skimmed.*

This rule has its limitations. One limit to its use as a guide in sorting out milks that merit detailed examination can readily be shown when the line representing the minimum legal standards in Pennsylvania<sup>11</sup> is plotted on the same axes with it. To obtain the values necessary for plotting this line, equation (1) may be transformed as follows:

$$T = \frac{1}{4} L + \frac{6}{5} = 12\%$$

whence,

$$F = 10 - 0.20833 L \dots\dots\dots (13)$$

The values in the following table have been calculated by use of this equation (13):

TABLE II.

<i>Lactometer reading at 60°</i>	<i>% fat calculated by formula (13)</i>
27	4.4
28	4.2
29	4.0
30	3.7
31	3.5
32	3.3
33	3.1

Any of these calculated values of F is the least or minimum fat percentage to be expected in a (legal) standard mixed milk that has exhibited the corresponding lactometer reading. As an example, consider a mixed milk found to have a lactometer reading of 31. The minimum fat per cent. in such a milk if it is above (legal) standard, *i. e.*, if it contains not less than 12 per cent. of total solids, is 3.5 per cent. Should this milk upon analysis show less than 3.5 per cent. fat, it should be set aside for further consideration because it is not above suspicion of being sub-standard.

When the numerical values in Table I and II are plotted on the same axes, the lines marked I and II respectively on Fig. I are

<sup>11</sup> See footnote No. I.

obtained. The intersection of line II with I shows where the legal standard in Pennsylvania limits the use of the skimming rule. In the writers opinion it is much better practice in Pennsylvania for the analyst to limit himself in all possible cases to establishing that a given adulterated milk is sub-standard rather than to base the legal action upon the charge of skimming.

Another limit to the use of the skimming rule as a guide in sorting out mixed milks that merit detailed examination could also be readily shown were it possible to lay off on the same axes a line, III, representing the limits separating the watered milks from the unwatered milks, among those that lie above the legal standard. Here the data are less satisfactory than in the two other instances. But the writer has used, tentatively at least, a suggestive formula due to Bialon.<sup>12</sup> It may be urged with reason that it does not rest upon American experience, but Bialon's formula may be not only suggestive but also useful to some degree until such time as American experience may have shown that Bialon's constant for the gravity of unwatered fat-free milks is different from or is the same as the corresponding constant exhibited by the outputs of large numbers of American herds.<sup>13</sup>

Bialon's formula is

$$\text{Specific gravity of the fat-free milk,} \\ M = \frac{100 G - F}{100 - F/0.933} \dots\dots\dots (14)$$

He places the lowest gravity in unwatered fat-free milks at the figure 1.0323, hence for the poorest unwatered milks his formula may be written

$$1.0323 = \frac{100 G - F}{100 - F/0.933} \dots\dots\dots (15)$$

Substituting in equation (15) the value of G as given in (5), and reducing, Bialon's formula becomes:

$$F = 969.927 - 939.579 G \dots\dots\dots (16)$$

The values in the following table have been calculated from this equation (16):

<sup>12</sup> *Milchwirtschaftliches Zentralblatt*, I, 1905, p. 363. See Barthel, *Die Methoden zur Untersuchung von Milch und Molkerei Produkten*, 1911, p. 134.

<sup>13</sup> As already suggested in footnotes Nos. 3 and 5, practically every milk formula has been put forth first in a form that was tentative or was later modified.

TABLE III.

<i>Lactometer reading at 60° F.</i>	<i>% fat calculated by formula (16)</i>
26	6.0
27	5.0
28	4.0
29	3.0
30	2.0

When by the aid of the data in Table III, a line III, is laid off on the same axes as were previously used (see Fig. 1), the intersection of line III with line II shows within what limits Bialon's formula is suggested for use in the method herein proposed. Within these limits, any calculated value of F is the least or minimum fat percentage in a mixed milk that is above suspicion of watering and that has exhibited the corresponding lactometer reading. As an example, consider a milk found to have a lactometer reading of 27. The minimum per cent. of fat in such milk if it is above suspicion of being watered is 5 per cent. Should this milk by actual analysis be found to contain less than 5 per cent. of fat, it should be set aside for further consideration.

Considering now the completed graph shown in Fig. 1, the area that lies above the broken curve formed by the intersection of lines I, II and III contains all pairs of values of lactometer and fat to be found in the mixed milks that in routine work may be passed by the analyst. The area below the broken curve contains the rest. Hence in the course of routine milk examinations if the values found for L and F be located by the analyst on Fig. 1, it becomes a simple matter to set those milks that are suspicious apart from those that may be passed.

It is not essential that a Quevenne lactometer be used in the work, although it is more convenient.<sup>14</sup> The specific gravity can be found more accurately and almost as quickly with a Mohr-Westphal specific gravity balance. The result thus obtained is readily converted into Quevenne degrees by formula (4). Since  $L = 1000 G - 1000$ , then, for example, if the gravity is found to be 1.029 the corres-

<sup>14</sup> An excellent form of Quevenne lactometer is that recommended by Shaw & Eckles, l. c. footnote 5; but it contains no thermometer. The common form in use is an improvement made by Müller on the original Quevenne lactodensimeter. See Müller, *Prüfung der Kuhmilch*, 1877.

ponding Quevenne reading will be 29. The figure for the specific gravity thus gives at a glance the corresponding Quevenne figure. But no Mohr-Westphal balance outfit should be depended upon until it has been proved to meet the following requirements: (1) the weights of the riders must be in the proportion of 1 : 10 : 100 : 1000; (2) the divisions on the beam must be at equal intervals; and (3) the outfit must show in water of some known temperature the density water is known to possess at that temperature.<sup>15</sup>

If a New York Board of Health lactometer<sup>16</sup> is used, its reading need merely be multiplied by 0.29 in order to learn the corresponding Quevenne reading, for 100° Board of Health = 29° Quevenne.

In any event, fluids of known specific gravity should be available for calibrating the instrument used. In dealing with this matter, a most important point to be borne in mind is that while most specific gravities are referred to water at 4° C., lactometer readings relate to gravities at 60° F. referred to water at 60° F.<sup>17</sup> When the centigrade scale is used, the density  $D_{60^{\circ}\text{F.}}^{60^{\circ}\text{F.}}$  is usually taken as identical with the density  $D_{15^{\circ}\text{C.}}^{15^{\circ}\text{C.}}$ . The writer has found solutions of sulphuric acid and solutions of sugar useful for such calibrations.

Sulphuric acid is better adapted to use by a chemist than by others. It is desirable to be able to prepare solutions by their normalities, such that their specific gravities will correspond to certain points on the lactometer scale. To this end I have calculated the values for the constants in the following approximation formula within the range of specific gravities from 1.014 to 1.041:

<sup>15</sup> Kohlrausch, Tr. *Physical Measurements*, 1894, p. 45.

<sup>16</sup> This is sometimes called the Spence scale. "The two fixed points on the scale of this instrument are the 0° mark which is at 1.000 the specific gravity of pure water, and the 100° mark which is set at 1.029, the minimum gravity of milk. The graduations are continued to 120° and 130°. The point 1.029 which was long ago fixed in Europe as the limit of the density of genuine healthy milk was redetermined in 1875 and 1876 by the health authorities of New York and New Jersey, from actual experiments at the dairies. Out of 1600 cows whose milk was examined, only six, two of whom were sick at the time, were found to give milk below that figure." Pellew, *Man. of Prac. Med. and Physiol. Chem.*, 1893, p. 178. Every degree below 100° was supposed to represent one per cent. of added water. No such interpretation of the reading of the Spence scale is today acceptable.

<sup>17</sup> The correction for temperatures other than 60° F. may be gotten from any book dealing with milk analysis; for example, Leffmann's *Milk Analysis*, cited in footnote 5.



$$N = A + dB + d^2C + d^3C + d^4E + \dots$$

where N = the normality of the sulphuric acid

d = the specific gravity  $D^{15^\circ\text{C.}}$

$$A = -297.800$$

$$B = +916.349$$

$$C = -1047.430$$

$$D = +506.431$$

$$E = -77.5467$$

It is better to use a six-place logarithm table in applying this approximate formula.

For more general use, cane sugar is suggested, because in the form of the best grades of granulated sugar it is easily obtainable and is cheap. A solution of any desired percentage can readily be made by weighing off the proper quantities of sugar and water.

In Table IV are given the proper normalities of sulphuric acid and the proper percentages of sugar for obtaining solutions for use in calibrating, such that they will have specific gravities located at every five degrees along the Quevenne scale. The normalities of the sulphuric acid were arrived at by application of the approximation formula already given, after deriving it from the table to be found in Landolt, Bornstein, Meyerhoffer *Phys. Chem. Tabellen*, page 326. The percentage of the sugar solutions were worked out from the same source, page 364, checked by values in *Tables Annuelles Internationales de Constantes et Données Numériques*, page 17. In all of these operations due attention was given to the fact that the tables give densities that are not on the same temperature basis as the densities of milk (otherwise table 10, p. 389, *Methods of Analysis Of. Agr. Chemists*, 1919, could be used). After sugar solutions have been made, if there is any doubt about them they may of course be checked by the polarimeter or by the refractometer.

TABLE IV.

<i>Specific gravity at 15° C.</i>	<i>Lactometer reading</i>	<i>Normality of sulphuric acid</i>	<i>Percentage of sugar solution</i>
1.0200	20	0.618	5.065
1.0250	25	0.771	6.307
1.0300	30	0.929	7.537
1.0350	35	1.087	8.755
1.0400	40	1.240	9.963

## SUMMARY.

A direct method has been described for sorting mixed (herd or market) milks into two classes, those probably adulterated or sub-standard and those probably neither adulterated nor sub-standard. The kinds of adulterated milks considered are those that are skimmed and watered. The method gives preference to the establishment of sub-standard character whenever possible, with skimming and watering as abuses to be dealt with by detailed analysis only when the adulterated milk is above the legal standards. The simplest way to use the method is graphically,<sup>18</sup> though a very simple skimming rule is given for use within certain limits. The fundamental values in the method have been arranged to be the lactometer and the fat, because they are the two values determined at the outset in routine work. A table is given for the calibration of lactometers.

## SCHOOLS OF PHARMACY AS PRE-MEDICAL SCHOOLS.\*

BY HORATIO C. WOOD, JR., M. D.

*Professor of Materia Medica at the Philadelphia College of Pharmacy and Science.*

Forty of the States in our Union demand as a prerequisite to the study of medicine one or more years of "college education," *i. e.*, a study of subjects beyond the high school standard. It is specified in many of these laws that this education must be acquired in a "college of arts and science." Although the wording of this section of the laws is sometimes ambiguous the manifest purpose of

<sup>18</sup> The graph as given in Fig. 1 can readily be modified for use in States which, like New York and New Jersey, fix the minimum legal limit for total solids at 11.5 per cent. instead of 12.0 per cent., as in Pennsylvania. The only effect of the change will be to drop the line II to a position parallel to its present one but nearer to the origin of the axis. Similarly, line III can be moved nearer or further from the origin as experience may dictate. Neither of these changes modifies the principles upon which the proposed method rests. For practical use in the laboratory, the graph is best plotted from Tables I, II and III upon paper cross-ruled in inches and tenths of inches.

\*Read before the Philadelphia Branch of the American Pharmaceutical Association.

it is to exclude those schools where professional preparation has been the prime purpose. The University of Pennsylvania says: "Time spent in professional schools of law, dentistry, pharmacy, etc., will not be accepted as the equivalent of any part of the two years of college education."

I should like to have you consider with me for a little while this evening whether this discrimination against schools which teach pharmacy is a wise one.

#### REASONS FOR COLLEGE EDUCATION.

Before undertaking this investigation we should have a clear idea of why collegiate preparation is desirable for the study of medicine. As I see it there are three fundamental reasons.

*First.*—Weeding out the mentally incompetent. In an interesting article in the *Scientific Monthly* (January, 1921) Professor Pillsbury, of the University of Michigan, points out that the modern educational system has a "very important function as a selecting agency, a means of separating the men of best intelligence from the deficient and mediocre. All are poured into the system at the bottom; the incapable are soon rejected or drop out after various grades and pass into the ranks of unskilled labor . . . the more intelligent who are to be clerical workers pass into the high school; the most intelligent enter the universities, whence they are selected for their professions." There can be no doubt that the amount of education a man can acquire is limited by his natural endowments. There are types of intellect, amply sufficient for the requirements of swinging a pick-axe or shoveling coal, to whom an asymmetric carbon atom would remain a mystery even after forty years of study. It is manifest that a man with insufficient degree of intelligence to pursue a course at college can never reach high success in the practice of medicine.

*Second.*—Advantage of a certain degree of familiarity with what are called "cultural" subjects. A man may be able to cure malaria without ever having read Shakespeare, but he is certainly limited in his outlook on life and, I believe, in his usefulness to the community unless he has some acquaintance with English literature.

It is highly improbable that he who has never read any of the standard masterpieces will ever develop a good literary style either in speaking or writing. When I say "good literary style" I mean the power of expressing himself so as to convey his meaning clearly and forcibly, not merely to charm the ear. If a man be ignorant of history he cannot properly interpret modern trends either in his profession or in the world in general and there is certainly a crying need in the medical profession today for men whose feet are held to the ground by a knowledge of the fads of the past. But I am not here to argue for the value of general culture as a professional asset; I can only say that, like the great majority of professional educators, I am firmly convinced of it.

*Third.*—The third, and probably most important reason for the pre-medical course is to provide a knowledge of certain branches which are fundamenal to the medical sciences.

#### COMPARATIVE ADVANTAGES OF SCHOOLS OF ARTS OR OF PHARMACY.

Let us consider the advantages of the present pharmacy course as a preliminary for the medical course under these three divisions.

First as a mode of selection of the mentally fit. The value of the present pharmacy course as a means of separating men into their intellectual or psychological groups seems to me at least equally high, if not higher, than that of the ordinary college curriculum. The subject of materia medica is as good a test of a man's memory power as that of history. Organic chemistry requires a degree of logical reasoning of as high a type as that in trigonometry or calculus. The man's powers of observation, as well as his control over finer muscle movements, are fully tested in the chemical and pharmaceutical laboratories. I might digress a moment to point out that motor control, *i. e.*, the power to guide accurately the finer movements of the hands, is regarded by psychologists as an important test of intellectual capacity and is an essential quality both to the student and practitioner of medicine. The success of the medical student in anatomy, physiology, pharmacology and chemistry is very largely conditioned on his ability to perform delicate manipulations.

The second advantage of a pre-medical college training is a widening of the mental horizon that comes only from knowing something of matters beyond the realm of our daily occupations. The relative value of various studies for this purpose is a matter of per-

sonal opinion, but I wish to point out that the differentiation of a purely cultural subject rests primarily upon the fact that it has no immediately apparent usefulness in assisting a man's professional activities. Whether a subject is a cultural one or a utilitarian one depends very largely upon what the student's future career is to be; for example, a knowledge of trigonometry is of no immediate advantage to a practicing physician but is essential to the engineer; to the one it is a matter of general educational interest, to the other it means bread and butter. To the business man Grecian history is purely an ornamental acquirement but to the artist it is almost a professional requisite.

While some of you may differ, the subjects which seem to me pre-eminently suitable as educational ornaments for the physician are rhetoric and history. I also believe that he should be well grounded in at least two foreign languages, one ancient and one modern, and that a knowledge of higher mathematics, as trigonometry and calculus, is valuable. I do not wish to infer that other subjects such as geology, psychology and botany may not be of value as educational embellishments but they are rather too closely related to the professional subjects to be considered as purely ornamental.

It is very manifest that the ordinary two-year course in pharmacy is so hopelessly deficient in these branches that it lies outside of all comparison with the academic institutions. There has recently been, however, a strongly manifest tendency on the part of colleges of pharmacy to enlarge the scope of their work, and a number of them have instituted courses covering four years of study and leading to a degree of Bachelor of Science in Pharmacy. In these institutions are being offered, although not in so abundant variety as in the academic colleges, courses covering the more essential topics of a liberal education such as English, French, German and mathematics.

The third reason for requiring a collegiate education is that there are certain branches fundamental to the medical sciences, which are no longer taught in medical schools, which are essential to understanding of the medical subjects. For example, it is manifestly impossible for a student to follow the course in physiological chemistry, which is usually given in the first year of medical curriculum, unless he has an acquaintance with general chemistry.

That this is the most important reason for pre-medical training is shown by the fact that a knowledge of the same fundamental branches is required, not only by the Council on Education of the

American Medical Association, but practically all the medical schools in the country and also by the laws governing medical practice in a majority of the States in the Union.

Thirty-six of the United States require two years of college education as preliminary to the study of medicine, and four others require one year of college education. Of thirty-one States, of whose requirements I have record, twenty-seven specify that a portion of this preliminary education must be devoted to the subjects of physics, chemistry and biology and sixteen of them include also a modern language. In only four of these thirty-one States is there no restriction as to the subjects to be studied. The rules of the Council on Education of the American Medical Association require, in addition to a high school education, two years in an "approved college of arts and science" which must cover a minimum sixty semester hours and include a certain number of hours in specified subjects. These are shown in Table No. 1, column 1. In addition to the obligatory subjects mentioned in this table the Council on Education "strongly urge" that a portion of the elective time be devoted to a foreign language, botany, zoology and psychology.

As an example of requirements which are distinctly in excess of the minimal outlined by the Council on Education we may take the entrance requirements of Johns Hopkins University. There are other schools in the country whose entrance requirements are as high or even more strict than that of Johns Hopkins but I have chosen this school because, while it does not insist upon a collegiate degree, it requires an amount of preliminary education which cannot be finished in two years. The conditions for entrance into Johns Hopkins University Medical School are shown in column two of the table.

In order to ascertain how nearly these conditions of preliminary education may be fulfilled in a college of pharmacy, I have summed up the amount of time devoted to the various subjects which are either requisite or highly desirable as a preliminary to medical study, in the first two years of three schools of pharmacy which offer a four-years' course leading to the degree of Bachelor of Science in either pharmacy or chemistry. The curricula of these three schools, which are fairly typical, have been tabulated in the columns marked 1, 2 and 3 in the table.

TABLE I.

	<i>A. M. A.</i>	<i>J. H. U.</i>	1	2	3
Physics	8	10	8	8	8
Chemistry	12	15	38	23	18
Biology	8	11	†10	0	0
Foreign Language	*6-12	A	10	12	8
English	6	0	10	6	4
Pharmacy	0	0	10	8	11
Botany	*3-6	0	0	4	2
Pharmacognosy	0	0	0	4	9
Mathematics	*3-6	0	6	6	4
Others	26	B	8	0	2
Totals	60		100	71	66

It will be noted in the above table that the courses in all these schools meet or exceed the minimal requirements of the Council on Education except in the subject of biology, and in one school also in English. In school No. 1, which apparently meets all the requirements of the A. M. A., it is impossible to ascertain from the catalogue whether or not it meets the requirements in biology because no separation is made between the amount of time given to biology and to botany. While botany, strictly speaking, is a branch of biology, the Council on Education draws a line between general biology, botany and zoology; the rules state that the requirements in biology may be "satisfied by a course of eight semester hours in either general biology or zoology or by courses of four semester hours each in zoology and botany, but not by botany alone."

It is evident, therefore, that however we may feel upon the advisability of a student acquiring his pre-medical training in the schools of pharmacy, some modification of these courses is essential to conform with the legal requirements in most of them. It is probable, however, that these schools would have little difficulty in expanding their biological courses.

\*These subjects not compulsory, but "strongly urged."

† Includes Botany.

A. "A reading knowledge of French and German" required.

B. Must have had Latin as far as four books of Cæsar.

A. M. A. = Minimum requirements of the Council on Education of American Medical Association.

J. H. U. = Johns Hopkins University, entrance requirements.

It seems to me evident that the course leading to Bachelor of Science in pharmacy is, at least from the legal standpoint, with perhaps some modifications, capable of being used in the training of medical as well as pharmaceutical students. The question, however, of the relative desirability of obtaining this introductory knowledge in a college of so-called liberal arts or in a college of pharmaceutical science is one that involves many more features than the mere amount of time devoted to specified subjects.

#### ASSERTED SUPERIORITY OF COLLEGES OF ARTS.

The most concise statement that I know of, as well as authoritative, on the advantages of collegiate training, is that of Dr. Colwell, secretary of the Council of Pharmacy and Chemistry of the American Medical Association.

In an address before the Annual Congress of Medical Education last year, Dr. Colwell (*Journ. A. M. A.*, March 13, 1920) sums up:

"The advantages in requiring that the pre-medical work be taken in approved colleges of arts and sciences are:

"1. The physics, chemistry and biology are taught without reference to their special bearing on medicine. It is not known today what particular facts obtained in the study of these sciences will be most useful in the medical research of tomorrow.

"2. The quality of the pre-medical work is assured since it is carried on in courses leading to the degree of Bachelor of Science in reputable colleges of arts and sciences. This provides also a satisfactory standard for measuring the value of irregular or so-called 'equivalent' courses.

"3. The student is free to make a final choice of his life-work until he is best qualified to do so. He enters the classes leading to the science degree; he has a chance to compare notes with those studying for other callings, and may find that some other line of endeavor appeals to him more than medicine. If so, he can make the change without any loss of time, since his pre-medical courses are equally acceptable for admission to other departments. This freedom of choice is of great importance to the students, since from 10 to 30 per cent. change to some other calling before their two-year course is completed.

"4. Students now enter medical schools with the benefit of two years in the college atmosphere, the contact with students in other departments, the social life, and the athletics, which are bound to influence their entire lives.

"5. The arrangement is a safeguard against medical cults. It is



seldom that a student who had studied genuine science in his courses in physics, chemistry and biology will be misled by the fallacious claims advanced by unscientific cults."

On each of these arguments I should like to say a few words.

*First.*—That the physics, chemistry and biology are taught without their special bearing on medicine.

While I confess I cannot see great weight in this argument, it would be true, at least in a degree, of a course in a college of pharmacy and science. If the biology in such an institution were taught with any bias at all it would be as introductory to botany, a subject which is not recognized in our modern medical curricula.

*Second.*—That the quality of the pre-medical work is assured since it is carried in the courses leading to the Bachelor of Science in reputable colleges of arts and sciences.

The crux of this argument, of course, lies in the B. S. degree. If a college of pharmacy is prepared to and does give a B. S. degree, after a standard four years' course, is it not just as "reputable" as an academic institution that does the same? Why should the fact that one institution teaches philosophy and Greek, and the other pharmacy and materia medica, beside the science courses, militate either for or against their respectability?

*Third.*—The student is free to make a final choice of his life work until he is qualified to do so.

This means that when the student has entered the science course of a college he has not definitely committed himself to the study of medicine. If, however, at the end of one or two years of the college course which he has arranged as preparatory to the study of medicine, he decides he will become an engineer or an architect, he will have wasted a good deal of his time in studies that are of no direct value to him. But the chemistry and biology that he would learn in a college of pharmacy are just as useful to the lawyer as the chemistry and biology that he would learn in a college of art.

*Fourth.*—"The benefit of the college atmosphere, the contact of students in other departments, the social life and the athletics."

I confess that I am somewhat peeved whenever I come across this hoary tradition that association with your fellow man in a col-

lege hall has a different effect upon your character than association with the same man under any other circumstances. I believe the contact of the young man with his fellows is good for his development, but why that contact has to be sanctified by an ordained college of arts of science seems obscure.

As for the social life of a college that is a thing which varies with the individual school, not with the class of institution. When we contrast, for example, conditions at a great university like Columbia—with its thousands of pupils, relatively few of whom are in residence at the college, contending with the distractions of a great city in whose midst it is situated—to those at a little college like Haverford—located in almost rural surroundings, with its two or three hundred pupils practically all of them living on the campus—it seems ridiculous to talk about the atmosphere of college life as a fixed entity. If we grant for the sake of argument that there is some advantage to a boy being thrown into such intimate contact with two or three hundred of his fellows that he comes to know most of them by their first name, evidently it is not to be obtained in a large metropolitan university; on the other hand, if we believe that there is some advantage in having a common interest with two or three thousand fellows of his age with most of whom he has not even a nodding acquaintance, obviously, he cannot reap that benefit at any one of the hundreds of small colleges scattered throughout the country.

The “atmosphere” of the college class room is only too often still that of school-boy days: “If I can fool the teacher (or in this case professor), into believing that I have done work that I have not done that proves how smart I am.” It does not seem to enter the mind of the pupil that he is there for the purpose of acquiring knowledge which is going to enable him to earn his living and to take his place among the workers of the world.

In striking contrast to this, in a college of pharmacy and science the presence in the class of men who are engaged in direct preparation for their life work helps to awaken a realization in the whole student body that play-days are for children, and to engender an atmosphere conducive to serious study. This mental attitude as well as the knowledge actually acquired, is a valuable asset to the student of medicine.

*Fifth.*—The arrangement is a safeguard against medical cults.

I can conceive of no atmosphere so hostile to the development of a medical cult as that of a college of pharmacy; I would not except from this statement even the halls of a medical school. Medical science is still based largely on theory; pharmacy is cold, indisputable facts and the man who has become accustomed to handling facts does not fall an easy prey to the weird speculations of the fad-dists.

There is one advantage that a college of Arts has over one of Pharmacy which appeals to me strongly; and that is the larger variety of secondary subjects offered to the student. Out of a required total of sixty semester hours the Council on Education insists on definite assignments for only thirty-four hours. In other words, nearly half of the student's course may be arranged to suit himself. If he be interested in history, or geology, or philosophy, he has a certain amount of time which can be devoted to these scholastic amusements. The Pharmaceutical school, however, offers him but little in the way of diversion, pharmacy, mathematics and Latin is about the sum total.

While, in all candor, we must acknowledge this is a real deficit, I feel that there are certain superiorities of the school of pharmacy and science which offset it.

Of the three fundamental subjects whose necessity is recognized by every one, there can be no question that the most essential is chemistry. It must be remembered today that in most medical schools there is absolutely no instruction in the subject of general chemistry; it is as much taken for granted that the student knows this subject as it is that he knows how to add and multiply (to be sure, I have met medical students, not a few, who were unable to work simple problems in percentage, but, they are laboring under a great disadvantage). A fair knowledge of general chemistry is an absolutely necessary antecedent to physiological chemistry, and the better the student is grounded in chemistry the easier it will be for him to gain a clear apprehension of pharmacology, physiology and many other branches.

I do not think that any one can seriously question the greater thoroughness of the chemical instruction given at a college of pharmacy and science compared to that of a college of arts and science. In the first place, if we compare, as typical, the number of hours

on the curriculum of college No. 1 we will note that there is three times the requirements of the Council on Education. Moreover, I am persuaded that the quality of the teaching is superior and this I say without derogation to the academic institutions. It is only reasonable to expect that a subject which occupies nearly one-third of the time of the students, and is taught by one-sixth of the faculty, of an institution should be more highly developed than at an institution where it forms a mere accidental or unimportant part of a great number of courses. Go out among the druggists and the doctors of the United States and see who has the better knowledge of chemistry! It is not merely because the druggist uses his chemistry, for I doubt if the pharmacist has much more need for chemistry in his daily occupation than the physician, but it is because the training in chemistry given in schools of pharmacy is more than equivalent to the entrance requirements for the medical school *plus* the chemistry taught in the medical school itself.

In physics and in biology the other two fundamental subjects, it is not unreasonable to suppose that the training will be at least equal, if not superior, in the school of pharmacy to that in the academic institution for the reason that both of these subjects are more or less fundamental to the subsequent course in pharmacy.

We see, therefore, that the college of pharmacy is superior to the college of arts in the instruction in the required pre-medical subjects and I wish to go further than this and to show that the college of pharmacy offers certain advantages even in the elective studies. It is notorious that the weakest part of the medical curriculum is in *materia medica*. Time after time medical writers have stated that the reason that the manufacturers of proprietary mixtures flourish like the green bay tree is because the physicians of this country realize their inability to write a prescription properly. There is no better way to learn how to mix drugs, and how not to mix them, than to see the actual results of various combinations. In other words, while I would not assert that a practical acquaintance with pharmacy is necessary for the writing of prescriptions, I do believe it is of valuable assistance. That most teachers of pharmacology agree with this view is shown by the number of medical schools which include a course on pharmaceutical manipulations as part of their regular studies. But the time given to this course in the medical curriculum is totally inadequate to teach anything but the merest

smattering of general principles. Even if we grant that the instruction in pharmacy in the typical B. S. course of the schools of pharmacy and science is more than is actually needed by the physician, it would require much argument to make me believe that a knowledge of geology or calculus is more valuable to a doctor than a knowledge of pharmacy.

We should perhaps bear in mind in this discussion the student who is willing to spend four years in order that he may have a college degree and give some thought to the senior years of a college of pharmacy and science. In some of the institutions of this nature there is considerable variety in the subjects that are offered in senior years. The student may fit himself, for example, for an immediate position in industrial chemistry, or for the practice of pharmacy in one of its numerous branches. If, at the end of his sophomore year he is still intent upon the study of medicine, he has offered to him a variety of subjects such as materia medica, bacteriology, pharmaceutical chemistry, etc., which will be of direct assistance in his future medical career, that are not obtainable in the ordinary college of arts and science.

In conclusion I may sum up my views in the statement that while the courses leading to Bachelor of Science in Pharmacy are comparatively new and not yet developed to their highest efficiency the day is not far distance when medical colleges and legislators will no longer be justified in their discrimination in favor of the college of arts and science as against the college of pharmacy and science.

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## SOME MUCH NEEDED CHANGES IN THE PRACTICAL EXPERIENCE REQUIREMENT OF MANY PHAR- MACY LAWS.

By LUCIUS L. WALTON, PH. G., PH. M., PHARM. D.

*President, National Association of Boards of Pharmacy.*

We have heard much of late in condemnation of the drug store experience required under our pharmacy laws, prerequisite to becoming licensed as pharmacist. A few writers would abolish this requirement altogether and substitute therefor a course in a college of pharmacy, while others, recognizing that the college does not and cannot replace the shop in every relation in which practical exper-

ience is essential, would have the candidate for license get a year of intense drug store training after graduation.

Some pharmacy laws make employment in a retail drug store, regardless of the kind of work performed, a qualifying prerequisite, but prohibit credit for practical experience in pharmaceutical work gained in other places. This is obviously unfair in more than one respect and is perhaps the strongest objection to the experience requirement of such laws.

The drug store, the college, and the hospital dispensary all afford opportunity to gain experience in pharmaceutical work directly related to the proper and safe conduct of the business of a retail drug store. In no single one of these places can the practical experience be acquired which a pharmacist should have. Therefore, our pharmacy laws should provide an experience prerequisite which is consistent in all respects with the pharmaceutical work carried on in these respective places. The experience which shall qualify should be that gained in pharmaceutical work only, and of such period of time as the economic conditions controlling the conduct of the drug business now may warrant.

When we consider carefully the changes in the kind and amount of pharmaceutical work performed in conducting the average retail drug store, from that existing when four years retail drug store experience was adopted in most States as *sine qua non* for admittance to pharmacy licensing examinations, and which requirement still prevails generally, a striking inconsistency in the requirement with present conditions is apparent.

Among the factors operating to reduce the actual pharmaceutical work performed in the store and, therefore, making so long a term of store experience unnecessary for proper qualifications for conducting the retail drug business, may be noted the following: Competition of manufacturing pharmacists and chemists in the production of official products, and their ready to dispense special formulas or prescriptions now so much employed by physicians; tablet and biologic medication; legal standards for pharmaceutical products which must be determined by assay; laws and regulations controlling the use of alcohol and narcotics; increased compensation of clerks; limitation in the daily hours of service caused by labor laws; and the chain store.

Obviously, these have wrought their influence, also, in making

it unprofitable for retail pharmacists to make very many products. Some have caused the elimination of a great deal of the present medicinal armamentarium of physicians from the pharmacists' sphere of work in the store. The result is a gradual, serious and permanent curtailment in pharmaceutical operations and consequent loss of opportunity to gain practical experience therein in a retail pharmacy.

Comparing the conditions which confront the person taking up pharmacy with what they were when the present four years' practical experience requirement was established, the enforcement of this long term now is also inconsistent. At that time, and for a number of years thereafter, the young man entering the service of a pharmacist was not required to have any definite preliminary education. He began his experience by sweeping the store, washing windows, soda glasses, bottles and utensils used by others in compounding. He ran the errands, charged the soda water and mixed syrups for the fountain, also waited on soda water customers, none of which service is of a pharmaceutical character, unless it be learning to clean the utensils properly.

A year of such work and he was allowed to fold seidlitz powders, help roll compound cathartic pills, grind and powder some drugs (pharmaceutical work but seldom done in the pharmacy any more), and bottle some commonly used household remedies. The proprietor began to teach him some titles and direct his studies, if the former had time and was sufficiently interested. The first two years of service afforded very little opportunity to gain experience in compounding, or to perform any real pharmaceutical work. This part of the experience was gained during the last two years of apprenticeship.

Under these conditions the fathers were right in demanding a long term of service that before its termination might provide ample time in which to acquire a proper practical experience in all work pertaining to the business, and making it pre-requisite to registration.

But we live in a different day. Those entering pharmacy are high school boys or girls. Some are high school graduates and all must be very soon. The college of pharmacy is the best place in which to get practical experience in performing pharmaceutical operations. The menial work of the store is being done more or less by persons who do not aspire to become registered pharmacists,

because it has become too costly for pharmacists to pay the wages demanded by educated persons and permit them to employ their time in such service. Graduation from a reputable college of pharmacy is the legal requirement for pharmacy licensure in nearly half the States, and we are fast approaching the day when this will be required by all.

These changes in the economic conditions affecting the business and practice of pharmacy, and the education of the pharmacist, call for adjustment of the practical experience prerequisite of nearly all pharmacy laws. More particularly, however, for States which have adopted the college of pharmacy graduation prerequisite. In the latter pharmacists must be persons who have been taught systematically the properties and uses of drugs and poisons, and the art of compounding them, in a school properly equipped for giving such instruction. This of itself warrants a considerable reduction in the term of store experience, for this teaching responsibility no longer rests upon the preceptor in its entirety and the time required under store conditions in which to do it may be deducted justly.

For candidates desiring registration as pharmacist a short term of practical experience could be adopted at once in a number of States, without lessening in any important relation the qualifications of a person intrusted with legal authority to conduct a pharmacy.

Present conditions in States having the college of pharmacy graduation prerequisite warrant the adoption at once of a two years' practical experience requirement, confined to actual pharmaceutical work, one year of which shall have been gained in a retail pharmacy under the immediate supervision and instruction of a registered pharmacist.

With such requirement provision should be made for crediting experience gained in the dispensary of a public hospital, or other institution, and in the hospital corps of the U. S. Army, or U. S. Navy, if acquired under supervision of a registered pharmacist. But as all phases of pharmaceutical experience connected with the operation of a retail drug store are not available in either of these places, and in view of the short term to be required, a reasonable difference should be made in the credit as compared with that allowed for experience gained in the retail drug store.



This may be done by fixing a year's work in a retail drug store as a definite number of hours and placing an arbitrary value for the time in terms of UNITS. Relative values may then be given, as seem necessary and advisable, for pharmaceutical experience gained elsewhere. Moreover, such a system of crediting practical experience provides a uniform and satisfactory method for crediting practical experience which may be acquired through a few hours' pharmaceutical work in a pharmacy each day, or week, while the prospective pharmacist is attending high school.

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## RECENT ADVANCES IN PHOTOGRAPHIC PROCEDURES.

BY HENRY LEFFMANN, M. D.

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Several interesting advances in photography have been made during the current year. Perhaps the most striking is the discovery by Lüppo-Cramer, of Munich, that some coal-tar colors will desensitize to a considerable extent without materially affecting the latent image, so that after exposure a plate can be immersed for a brief period in a solution of the color and then developed in a much brighter light than would be otherwise applicable. The color that has been found most satisfactory is phenosafranin, a red dye freely soluble in water. This is used in dilute solution (0.5 gram to 1000 cc.) the plate being immersed in it for about two minutes, rinsed, and developed. Ordinary plates may be developed by a feeble white light; panchromatic plates by a red light. The procedure has been found satisfactory for autochromes. The red tint imparted to the plate may be removed by washing, but in the case of autochromes the oxidation which is employed after the first development removes the color. A. & L. Lumière and Seyewetz, the active French investigators in this field, made extensive trials of other materials, especially coal-tar colors, but found none as satisfactory as phenosafranin. Curiously, it was found that apomorphia hydrochloride has a desensitizing action, but this is, of course, of no practical importance. Solutions of phenosafranin in water are now on the market under trade names. The French investigators just noted found that auran-

tia, a yellow dye-stuff, had a distinct desensitizing action, but practically only for plates that are not sensitive to red light. It was also found that the solution of aurantia in acetone, which was the commercial form first used, is decidedly irritating to the skin and the firm is now putting out a dilute solution in alcohol. It is not likely, however, that the phenosafranin will be displaced. For work with ordinary plates these desensitizers are not particularly valuable, but for work with autochromes and plates of wide range of sensitiveness, it is a great convenience to be able to work in an appreciable lighted room.

It has been incidentally found that phenosafranin is an accelerator of some developers and also a preservative of them. Formulas have recently been published in which phenosafranin is used in place of metol. Hydroquinone is especially stimulated by the dye. The quantity of dye used is small, but owing to the staining power, and the greater difficulty of observing the development in a colored solution, it is not likely that it will come extensively into use as a regular addition to the developer.

The subject of simultaneous developing and fixing, that is, combining the hypo with the developer has been brought forward rather prominently lately by some French workers. It is not new, having been described many years ago. Among the formulas given lately is one in which acetone is used, which is the only one with which I have had any approach to success. One French firm has put on the market a tube containing the materials for the procedure, but I have not had any success with it. The acetone procedure is objectionable on account of escape of acetone vapor from the bath during development, which is, of course, not only unpleasant, but dangerous.

Paper negatives have been introduced in Germany as a substitute for film and glass supports, both of which materials have increased enormously in cost. Paper negatives are not new, but have never been a prominent articles. In one of the older forms the paper was rendered translucent after the picture was finished and thoroughly dried by rubbing in castor oil, and skilful operators did very good work in this way. The German product is a gelatin film carrying the sensitive silver salt, so attached that after completion of the work and thorough drying, the film can be easily stripped off. As

this is very thin, it is possible to print it from either side, thus eliminating the double printing necessary in some cases to avoid a reversal of the relations of the picture. Two German firms are now furnishing these negatives and trial with one made by the Bayer Company and termed "Plattenfort" ("away with plates") gave good results. The opacity of the paper rendered development somewhat less satisfactory than with glass or film, but the gelatin stripped readily when the plate was dry. Great care must be taken not to remove it while appreciably moist as it will fold and adhere to itself. The lightness, comparative cheapness and ability to print from either side are advantages, but the low cost of glass and film negatives will restrict the sale of such of these products to countries in which such low prices do not obtain.

A revival of stereoscopy seems to be indicated. French photographers are especially active in the matter, and the current French photographic journals abound with advertisements of stereoscopic cameras some of which are very elaborate and costly. About half a century ago the stereoscope was very popular. A parlor was hardly thought complete without a box of views and a hand stereoscope.

A new developer, "Neol," has been lately announced by a German firm and is now in the American market. It is, of course, claimed that this practically eliminates the question of exposure, giving equally good pictures if this has been too little, too much or all right. Probably it has a wider range than those long used, but such claims are often subject to much discount. With the exception of metol, the importation of which is forbidden, the well-known Agfa products are now in full supply in the American market.

Considerable attention is being paid abroad to modification of projection apparatus to produce on the screen the appearance of solidity and perspective more strongly than by the usual methods, but no satisfactory result has as yet been obtained. Jenkins, of Washington, D. C., the well-known inventor of cinematographic apparatus, has recently perfected a machine for taking pictures at a very high speed.

## ABSTRACTED AND REPRINTED ARTICLES

### PROFESSIONAL TRAINING.\*

Being the Address Delivered by SIR DAVID PRAIN, C. M. G., C. I. E., F. R. S., Etc., at the Opening of the Eightieth Session of the Pharmaceutical Society's School of Pharmacy, Bloomsbury Square, London, W. C., on October 5.

Many learned bodies make arrangements for special meetings at which anniversary addresses are delivered. The custom is supposed to serve intellectual ends. This School follows a practice which resembles that custom. But there is here a variation in method which suggests another motive. The proceedings today have so far had a moral object; they have shown the advantage of the patience that begets perseverance. Perhaps what remains may be meant to test your ability to display for fifty minutes the patience that leads to forbearance.

If so, I must warn you the test may be severe, for I have no reason to think myself qualified to deliver an Inaugural Sessional Address before this Society at the opening of your School. My excuse for venturing to speak in the presence of the Society is that my work has led me to study the natural history of some of your *materia*, and that I have been much indebted to its members for assistance while so engaged. My only warrant for addressing the School is that I have been invited to do so. The honour of that invitation is appreciated the more because it is undeserved.

As my official duties included investigation of the sources of certain drugs and actual production of others, I am encouraged to ask you to regard me as one of yourselves. The memory of this privilege increases my regret that experience does not entitle me to discuss problems belonging exclusively to pharmacy. But the accident to which I owe some relationship with your calling has led to like intercourse with others. Perhaps some of the information so acquired may interest you, especially as the vocation, outside my own, with which this intercourse has been most intimate, shares with pharmacy a common and contemporary origin.

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THE ORIGIN OF GARDENCRAFT AND PHARMACY.

The student of pharmacy often has occasion to appeal to unwritten history. He realises that her evidence, if harder to decipher, is more reliable than the written word. Unwritten history assures us that the earliest preoccupation of primitive man was as to what he might eat and wear. When these needs were first felt, man relied on wild Nature to supply them. As wild supplies became inadequate, a rudimentary husbandry had to be devised. This took the form of gardening; the hoe and spade antedate the plough. Modern refinement in husbandry is accidental; the original purpose of the cultivation of food and fibre-plants was to remedy defects and errors in diet and dress.

Horticulture has, then, some reason when it claims to have been founded by the first canonical patriarch. You may admit that claim without conceding that gardencraft is an older calling than pharmacy. The wants that led to the evolution of tillage induced more than discomfort; early man developed disease before he began to dig. The help of pharmacy may have been a secondary necessity; steps to meet that need were taken first. Though pharmacy and gardencraft originated at opposite poles in one primitive field of purpose, both callings are the immediate outcome of the same early solicitude.

STUDIES AND CURRICULA.

A School like this is not made by the building which houses it, but by the training it imparts. It is therefore natural if your thoughts, on the opening day of a new session, turn to the studies before you.

This is one of the subjects regarding which I cannot speak from experience. That is an advantage. Instead of being left to form erroneous impressions, I am able to turn for authoritative information to the brilliant Inaugural Address delivered by the President of the Society five years ago. Regarding pharmaceutical training as a whole, your predecessors were then reminded that schemes for compulsory curricula in pharmacy have been proposed at different times. Provision has been made in them for an irksome preliminary assessment of the knowledge you may have gained at school, and a fateful final scrutiny of the results of your professional train-

ing. For the period between these two examinations, such schemes usually postulate three separate disciplines:—

- (1) A training in pure science;
- (2) A pupilage in pharmacy; and
- (3) A course of professional studies.

The President of the Society supplemented this interesting statement by explaining that in your School it had been the policy of the Society to reverse the sequence of the two preliminary disciplines. That circumstance is an encouragement to me. Much of my official work during thirty-five years has been overtaken with the help of horticultural colleagues trained in accordance with the policy so long observed by the Pharmaceutical Society. For sixteen years I have been closely associated with the training of student-gardeners in pure and applied science as a sequel to pupilage in the practice of their craft.

#### PROFESSIONAL TRAINING IN GENERAL.

The fact that the sequence of these preliminary disciplines has been the subject of thought on the part of your profession as anxious as that bestowed on the question by gardencraft may perhaps serve as my excuse if my remarks this afternoon relate to professional training in general.

Callings whose work involves the possession of "skilled hands" and a "trained eye" are often subjects of discussion as to the relative merits of "theory" and "practice." Though such comparisons are always legitimate, they are not often useful. They may, when instituted by members of the craft concerned, lead to improvement in practice and enlightenment as to principles. Critics to whom the practice of a craft is unfamiliar, display a tendency to think of "practice" and "theory" as being antagonistic. Experts in particular vocations know that, so far as their own work is concerned, conflict between "theory" and "practice" is impossible. Thanks to this saving circumstance, such discussions, even when they fail to do good, do no real harm.

There are certain crafts whose exponents seem to accomplish their allotted tasks without visible effort to master the principles that guide their acts. This does not affect the existence of these principles, and there is no calling in which the most consummate

master of its practice may not benefit by some knowledge of its theory. All of us, whatever our business may be, are indebted for our training to the same two teachers—Madame How, who tells us what to do in a given emergency; and Lady How, who enlightens us as to the true inwardness of her colleague's bidding. At the same time, although there is no vocation whose members can hope to "make good" until they have been fully instructed, the needs of most callings vary as to the extent to which acquaintance with their principles is essential, and as to the manner in which a knowledge of theory, as contrasted with practice, may be best imparted.

Even in crafts where a knowledge of underlying principles appears least essential, the question has another side. Every craftsman is the servant of his calling, with well-defined duties to it. But every calling has reciprocal duties towards its servants, who are entitled to take steps to ensure their fulfilment. In matters like this "Providence gives most help to those that help themselves," and there is no calling, whatever its nature or importance, whose members may not become better citizens if they think out the meaning of acts which habit, in their particular cases, has converted into "second nature."

#### VARIATIONS IN TRAINING: MEDICINE.

Modifications in training necessary at different times, and variations in training possible at a given time, are best understood if actual cases be considered. Medicine affords a good example of the one, husbandry of the other.

Public opinion insists that training in medicine shall go hand-in-hand with training in surgery. Though the duties in the two arts may differ, the law ordains that before a neophyte may practise either, he must be able to undertake both. The obligation to secure a "double qualification" involves complete professional training in the *fabrica* of surgery, the *institutes* of medicine, and the *materia* both arts share with pharmacy.

Originally, practical pupillage was the recognised procedure. It worked fairly well. The surgical *fabrica*, before the advent of antiseptics, were patent to the eye; success in practice depended on caution and manipulative skill. The medical *institutes* consisted largely of physiological and pathological postulates, which might be memorised; success in practice rewarded natural sagacity and saving

common sense. But pharmacy, when teaching intending practitioners how their *materia* should be used, incidentally proved to them how desirable it was that they should possess some acquaintance with chemical principles and with the characters and qualities of living organisms. When the *institutes* of medicine, discarding clinical authority, initiated the methods of direct observation and controlled experiment, students soon discovered for themselves that they could not grasp the facts underlying those subjective conceptions of the normal and the irregular they were expected to master, without some knowledge of physics and some understanding of the structure and functions of vital mechanisms.

Early journeymanship, originally spent at seats of learning discussing debatable questions and "wrangling" for degrees, was replaced by a system of "walking the hospitals." This developed into "a course of professional studies" which expanded at the expense of pupilage until the latter disappeared.

Medicine found that professional training gave better results than the practical instruction of pupilage, but that the opportunities for education, as contrasted with instruction, which pupilage affords, cannot be provided during a course of professional study. More was needed than a widening of the scientific foundation on which sound professional training rests. In order to "kill two birds with one stone" the "training in pure science" which future practitioners ought to undergo, was made a discipline distinct from the professional training which had to be imparted. The purpose was as sound as the theory on which it is based. But the extent to which it may be attained depends on the nature of the scientific discipline provided.

The policy interests you. Pharmacy sometimes pays it the compliment of advocating its adoption. This suggestion emanates from men of vision who foresee a time when, in pharmacy too, pupilage may be only a memory. When that day comes the need to follow medical example may have arisen. But while practical pupilage in pharmacy remains possible the need for a preliminary "course in pure science" is not clear, and the policy long adopted by the Society seems preferable. When Pharmacy has to devise a new policy, she may do well to study, rather than copy the example set by medicine. She may then, perhaps, avoid some far from trivial difficulties.



#### INSTRUCTION IN PURE SCIENCE.

When instruction in pure science forms an integral part of professional study, the principles of a science taught may be illustrated by facts connected with the calling the pupil is to follow. This involves some duplication; these facts must be referred to again when methods of practice are expounded. Such duplication possesses an educational value! it enables the same truth to be envisaged from different points of view.

Where instruction in pure science forms a prelude to professional training this advantage largely disappears. A decision has to be reached in advance whether scientific instruction be confined to the principles of a particular study or shall include the presentment of its salient facts. No middle course is feasible. The needs of different callings vary; it is not uniformly necessary that the master of a profession be an all-round scientific expert. Medicine and pharmacy, for example, do not think it essential that every future practitioner be as proficient in physics, chemistry, and biology as in his proper calling. Medicine believes that if her disciples can master the principles of these studies before professional training begins they may acquire familiarity with the special truths of each that bear on future practice, while being disciplined in the medical institutes. If this be true of those who practise medicine, it must also be true of competent teachers of medical practice. But it cannot apply to those who teach the institutes; such teachers, whether on the physiological or the pathological side, must be fully versed in physics, chemistry, and biology. Yet teachers of the institutes of any art should, like teachers of its practice, be recruited from among those who have studied that art and know its needs.

#### INTENSIVE TRAINING IN PURE SCIENCE.

When the institutes of medicine merely embodied the philosophical conclusions of clinical experience, no difficulty arose. Now that these institutes, like those of pharmacy, derive their inspiration directly from physics, chemistry, and biology, it is desirable that some who study medicine at a given time shall have made themselves as fully acquainted with the facts as with the principles of the sciences mentioned before commencing their professional course. There are few medical schools without any pupils who have undergone this intensive training in pure science. In some schools the

proportion of students so trained is steadily increasing. But their existence is due to idiosyncrasy; it is not the result of reasoned medical policy.

The effect of intensive preliminary scientific discipline becomes most marked during professional training in the institutes of an art or craft. Pupils who have only mastered the principles of the underlying sciences use the institutes as a means to the fuller understanding of practice; those disciplined in their truths display an inclination to serve the institutes. This is not unnatural. Some who find the physiological side of the institutes of medicine especially attractive show a tendency to omit the study of practice and to refrain from seeking a medical qualification. This is not from lack of interest in the diagnosis and treatment of disease. Much recent progress in both is due to the institutes rather than the practice of medicine; some noteworthy advances have emanated directly from those pure sciences on which physiology and pathology depend. The pathological side of the institutes now feels disposed to contend that neither in diagnosis nor in treatment can the surgeon or the physician be regarded as an expert.

Perhaps in leaving the provision of intensive preliminary training in pure science to hazard, medicine acts advisedly. The influence of such a training is subject to a potent limiting factor; the demand for physiologists and pathologists is restricted. Some who would gladly devote themselves to the service of the institutes feel compelled to study medical practice. This does not always modify their outlook. Disciples whose academic record might justify expectation of the highest rewards attending successful treatment of disease, devote themselves, after qualifying, to its prevention. They adopt this branch of their art, not so much because prevention was the primary purpose of medicine, as because medical investigation in this field is free from the philosophical shortcomings of clinical observation.

#### THE RAISON D'ETRE OF PRIMITIVE HUSBANDRY AND PHARMACY.

Alterations in outlook lead to modifications of policy. Primitive man, inadequately informed, distinguished health from sickness when he invented husbandry to maintain the one and pharmacy to alleviate the other. This archaic misunderstanding explains the belief, still at times entertained, that physiology and pathology

are "sciences." The logic of facts proves the institutes of medicine to be a homogeneous technology devised to apply physical, chemical, and biological truths; physiology and pathology are merely different aspects of one applied study. This new enlightenment has led medicine to revert to the strategy of early man, who regarded the maintenance of health as of more consequence than the treatment of illness. Unfortunately, the tactics primitive man adopted were not equal to his strategy.

Unwritten history tells us that the failure was not the fault of husbandry. When her hands were not tied by public opinion she gave evidence of her belief that the best way to prevent sickness is to destroy disease. The rustic simplicity of her methods did not lessen their scientific validity. As civility developed, the efficacy of the bonfire and the poleaxe in eradicating murrain and blight from herd and crop so impressed the community at large that they were copied by those in authority. The one was long applied by the Church to eliminate schism; the other is still at times employed by the State to extirpate faction. But as urbanity increased, public opinion manifested a dislike for their use in destroying human disease. This unreasoned objection did not modify the outlook of husbandry; satisfied that her policy was sound, she declined to preach a more comfortable doctrine.

#### THE BEGINNINGS OF MEDICINE.

Inability to shake the conservatism of husbandry was not the only difficulty early civilisation had to contend against. Pharmacy had originated as a craft directed first to warding off spells and afterwards to countering their effects. The pejorative significance of the Greek name for a member of your profession shows, however, that when historical chronicles began, an impression prevailed that pharmacy had gone over to the enemy. Unwritten history makes no suggestion of the kind; the belief, so generally entertained when culture dawned, that a pharmacist was necessarily a sorcerer and a poisoner, only proves that the effect of propaganda on public opinion was as powerful 4000 years ago as it is today. However this may be, early civilisation, unable to follow the advice of husbandry, ought to depend on that of pharmacy, was led to invent medicine, an art, the lexicographer tells us, "directed first to the prevention of diseases and afterwards to their cure." Limited to

defensive tactics, the new art at first hardly appreciated the strategy to which her evolution was indirectly due. With tireless zeal and constant courage, medicine, in the field of practice, has striven for four millenia to prevent sickness on defensive lines. But history delights to repeat herself, and medicine, apprised by her institutes as to man's original strategy, has at last adopted the tactics of husbandry. Passing from the defensive to a vigorous offensive, she now attempts to abolish disease.

#### THE SPHERE OF PHARMACY.

The secondary object of medicine being the cure of disease, pharmacy was no longer called upon to alleviate its symptoms. But pharmacy still had to supply the necessary *materia*; hence the friendly relationship between the new calling and the old, which teaches mankind how misleading propaganda may be. But while both callings are equally concerned with the virtues of their *materia*, pharmacy, with the wisdom which is one of her outstanding characteristics, concentrates her attention on their "qualities," and leaves medicine to study their "uses." On this scientific basis the respective responsibilities of the two professions towards their common *materia* are at present clearly defined. Should the new policy adopted by medicine succeed, some further adjustment may become necessary; its success may end medical practice and convert these *materia* into historic lumber.

The hope that the new medical dream may be fulfilled explains, though it does not justify, the complaint that pharmacy with her *materia* retards the advent of a sanitary millennium. Enthusiasm, even when infectious, hardly replaces fact. Already we hear warnings as to the risk we run when we carry sterilisation too far. We have, besides, to reckon with a system of public instruction which inhibits education so effectively that a constant supply of "conscientious objectors" to hygienic enactment is assured. Pharmacy, moreover, has powerful allies in chemical industries, with synthetic products to push and a subsidised reclamatory organisation. This may explain why "prescribing" and "dispensing" are not yet penal offences. This chemical support creates a risk that the "natural" *materia* of pharmacy, even if they remain officinal, may fall out of use, for medical fashion differs mainly from the sartorial kind in

its greater susceptibility to the influence of propaganda. Fortunately, it is equally fickle, and the danger may prove less instant than it seems.

#### TRAINING IN HUSBANDRY.

The question of training in husbandry differs from that in medicine, because gardeners and farmers decline to accept the medical view that practical pupilage is no longer necessary. But the question has given rise to two schools of thought. Many are still satisfied that practical pupilage affords all the training required. Others, whose watchword is "practice with science," believe that a course of training in pure science is desirable. But, unlike medicine, husbandry imagines that to impart such a training before professional instruction begins is "to put the cart before the horse." Whether in this, husbandry be right or wrong does not now concern us. Nor would it be safe to deduce either that husbandry has given less thought to professional training than medicine, or that medicine has reached conclusions sounder than those of husbandry. It is sufficient to remember that "circumstances may alter cases."

#### THE METHODS AND SCOPE OF HUSBANDRY.

It was no great merit on the part of husbandry to have realised in prehistoric days what medicine has only now discovered, that the surest way to prevent sickness is to abolish disease. Husbandry could employ methods medicine might not use. Nor is husbandry so conservative as early civilisation imagined. She knows quite well that whatever its ultimate benefits may be, the eradication policy is not conducive to immediate economy. She now prefers those newer modes of eliminating disease the medical institutes have devised. At the instance of her own institutes, husbandry at times takes the apparently retrograde step of attempting to treat where she used to destroy. Where, however, husbandry deserves credit is as regards the training she imparts to disciples destined to serve the institutes of husbandry as apart from its practice. These she subjects, as a matter of policy, to that intensive training in physics, chemistry, and biology, which in the case of those destined to serve the institutes of medicine is left to accident.

Within husbandry, however, horticulture and agriculture hold divergent views regarding technological advice. Horticulture, more

influenced by tradition than her younger sister, is indisposed to accept this from other than masters of gardencraft. Agriculture, taught to think she breathes a more enlightened atmosphere, does not urge her technological advisers to undergo practical pupilage in farming. A prejudice is not always unhealthy. Horticulture escapes the waste of time and effort occasionally experienced by agriculture owing to the consequences of defective tilth being mistaken for signs of disease. This type of mischance is one your profession must guard against when it comes to render sanitary science the assistance it now accords to medical practice. If the existing attitude of pharmacy, as contrasted with that of medicine and agriculture towards preliminary training in pure science be maintained, the risk in her case should be small.

Husbandry, like medicine, thinks her practice calls only for a training in the principles of the sciences that underlie its theory. But while husbandry never imparts such a training before professional instruction begins, those who arrange her curricula are divided in opinion as to whether the course in pure science, which all regard as desirable, may accompany or should follow practical pupilage.

#### THE CURRICULA OF AGRICULTURAL AND HORTICULTURAL SCHOOLS.

The curricula of most schools of agriculture are well adapted to the needs of those who have already mastered the craft of practical farming. In some cases, however, they reveal a belief that professional instruction, imparted concurrently with a training in scientific principles, may replace practical pupilage. But recent ordinances governing the work of such schools indicate that this belief has begun to waver; entrance is to be forbidden in future to those who have not already undergone a prescribed minimum of practical training.

The curricula of some horticultural schools seem also to manifest the hope that adequate practical and sound scientific training can be imparted simultaneously. But in gardencraft generally the belief is still held that the first business of the future gardener is to master his craft. Nothing, it is urged, should be permitted to impede or interfere with practical pupilage; only when this has been completed may inculcation of the principles that guide practice be undertaken.

#### FOUR TYPES OF TRAINING.

In callings like pharmacy or gardencraft we find, then, that there are, or may be, at least four distinct types of training. We may have practical pupilage alone; or we may have a training in pure science (1) as a prelude, (2) as a complement, or (3) as a supplement to practical pupilage. Let us consider briefly the leading characteristics of each type.

The part which pupilage unaided may play in the formation of character is perhaps less appreciated now than it once was. The first aim of pupilage is, by means of instruction and supervision, to make the pupil expert in his vocation. But where supervision is thorough the pupil undergoes education as well. Were this not so, pupilage might be almost as valueless as attendance at a school when games are forbidden. The system of teaching now prescribed has to subserve preparation for examinations. Teachers, through no fault of theirs, are largely limited to the task of imparting instruction, and the education their pupils obtain is mainly acquired unconsciously while at play. That the instruction given is good does not alter the fact that, where examinations must be prepared for, education suffers.

#### AN OBJECT-LESSON FROM THE EAST.

To supply evidence that pupilage may educate as well as instruct let me take you to the East. In an Indian botanical institution, where the horticultural officers were Europeans trained in science after pupilage in gardencraft, we had a staff of competent native gardeners. The needs of the institution being special, these gardeners had undergone pupilage there. That institution had been in existence over a century when, for the first time in its history, some of our most promising young native gardeners left to take service with an enterprising fellow-countryman whose business involved the use of sawmills and similar industrial appliances.

When asked what had led him to entrust gardeners with unfamiliar duties and pay them commencing salaries exceeding what they could ever hope to earn in their own calling, their new employer was quite frank. Good labour, he explained, was abundant; reliable supervision was scarce. At first his overseers were university graduates, trained in technical colleges. Yet there had been

accidents in his establishment. He had seen our men at work and thought their training had been good. "Since I employed your gardeners," he said, "there have been no accidents. They may know nothing about 'circular saws and steam-hammers,' but they carry out instructions and see that those under them do so."

But we need not go so far afield for evidence that pupilage alone may educate as well as instruct. The histories of pharmacy and gardencraft bear eloquent testimony to this. In both, the provision of a training in pure science, as apart from pupilage, is a thing of yesterday. The subject-matter of our Pharmacopœias and the contents of our gardens show that members of both crafts were addicted to observation and experiment, and were scientific workers without knowing it, before "natural studies" began.

#### SCIENCE BEFORE PRACTICE.

The arrangement under which a training in pure science precedes practical instruction is of interest to you, owing to its advocacy for pharmacy. In theory such an arrangement is admirable. The principles that underlie practice being already appreciated, the practice involved may be mastered more readily and with less delay. That the desired result is attained when the sciences have been fully mastered, there is no reason to doubt. Even in cases where only the principles of the sciences involved have been taught, advances in knowledge as well as mastery of the craft have followed. You know of such in the history of pharmacy; let me cite two from that of gardencraft. Hales as an undergraduate learned the principles of physics. Applying these to phenomena in his vicarage garden at Twickenham, he founded the study of plant physiology. Mendel, in the same way, applied the results of an early training in pure science when he founded the study of genetics in the monastic garden at Brunn. But in neither case were the scientific principles which led to such notable results acquired with the object of enabling these clergymen to improve natural knowledge or to master the practice of the craft they benefited. When a scientific subject is deliberately prescribed for the latter purpose, there is at times a tendency to think of its study in terms of some impending test. We can understand the relief felt when such an examination is over. But we can also understand, even if we disapprove, the tendency there sometimes is to forget not only the



anxiety but its cause. We know that the method of "science before practice" may be useful; that it is always of value we cannot pretend.

#### SCIENCE WITH PRACTICE.

The arrangement under which training in pure science goes hand-in-hand with practical instruction is also in theory sound. Here we hope to find practice illustrating the principles on which it is based, and science at the same time illuminating the application of these principles to practice. But the method violates an axiom applicable to most human affairs; it is usually best to do one thing at a time. What may and, at times, does happen is that pupils fresh from school and versed in the art of hoodwinking the enemies of education, put scientific principles acquired by rote to immediate use as mnemonics of manipulative details they may never have carried out. Where the destiny of such disciples is administrative or advisory, it needs the acid test of professional responsibility to show how specious an academic record may be. This, however, so far as the public interest is concerned, is a trifling disadvantage as compared with the moral effect of running practice and science in double harness, upon pupils whose interest in their proper calling is so intense that it absorbs most of their attention. These, in the examination room, at times fail to disentangle theory from practice: academic estimates of their attainments are apt to bear the relationship to reality which we might expect if ability to "ride to hounds" had to be judged by a horse-man's mastery of the "antics of the circus."

#### SCIENCE AFTER PRACTICE.

The arrangement under which a training in pure science follows practical pupilage is so familiar to pharmacy that little need be said of it. The result of thorough pupilage in gardencraft, where my acquaintance with its effects is most intimate, is to make the knowledge imbibed a part of the pupil's individuality. The comprehension of the sciences whose principles underlie the practice of the calling is therefore simple. Formal illustrations of the doctrines a teacher imparts are hardly needed; such illustrations are already latent in the intellectual equipment of the pupil. On occasions the truths stated by the teacher may appear to diverge from the experience acquired by the pupil; difficulties thus created can be sub-

mitted by the pupil, and resolved by the teacher, out of hand. The advantage of a training in pure science after pupilage is over, lies, therefore, in the fact that such a training is not a course of instruction at all. It is throughout an unbroken process of education, full of pleasure and interest, alike to teacher and taught. You have before you an enviable opportunity. Benefit by that opportunity; such another may never come your way again.

Whether at the close of such a course of training there be a testing examination is immaterial. The teacher knows that nothing of the kind is required. If, for purposes of professional registration, ordinance prescribes such an ordeal, it becomes, for the pupil, an incident devoid of anxiety. The candidate is aware that whatever an examiner may ask him he can only be requested to evince knowledge already part of himself.

#### FUTURE DEVELOPMENTS.

Should circumstances eventually compel pharmacy, as they have compelled medicine, to abandon practical pupilage, it will be interesting to see what course your successors adopt. If, when that day comes, your chief work be to aid the institutes rather than the practice of medicine, the preliminary discipline in science which precedes professional training proper must be of the intensive character imparted to the technological assistants of husbandry; a training in science such as is adequate for medical or agricultural practice will not be sufficient. In imparting the necessary training pharmacy may, as regards physics and chemistry, rely, as agriculture and medicine do, on the aid of academic science. But so far as the necessary discipline in biology is concerned pharmacy will do well to follow the example of gardencraft and impart the scientific training on her own account.

The reason is obvious. In the field of organic study academic science finds that, for purposes of doctrine, facts relating to the structure and functions of the animal and the plant as vital mechanisms are more useful than those connected with the natural history of living organisms. But in pharmacy, as in gardencraft, these truths, valuable and essential as they are, constitute only a portion of the knowledge a pupil must master, and pharmacy, like gardencraft, will find that in this particular field of study, if she wishes the work to be done adequately, she must do it herself.

SEEKING THE TRUTH FOR ITS OWN SAKE.

Whatever the method of training that prepares us to follow our calling may be, we must not conclude, when the course is over, that our training is then at an end. There is a sense in which it may be said that only then does real training begin. The facts of life, whether these be as pleasant as I would wish you to find them, or as stern as they prove at times to most, are inexorable. Their lessons cannot be evaded; we must all educate ourselves to accept them. But we can carry our education further than this. It is not what facts bring home to us, but what we can extract from facts that really counts.

It is this that Philosophy has in mind when she urges us "to seek truth for her own sake." It is this that History has in view when she advises us to "improve natural facts for use or discovery." It is this that Academic Science intends when she urges the prosecution of what she terms "original research."

Sometimes the process has the advantage of adding to our knowledge of natural things. But this is of small moment as compared with the opportunity it provides us of learning our limitations, and of attaining what the Greeks regarded as the highest of human ambitions—that of "knowing ourselves." When your professional studies are over, but not until then, try the expedient. It will bring you its own exceeding great reward.

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PLANT CONSTITUENTS.\* †

BY JOHN URI LLOYD, Phar. M.

CINCINNATI, O.

The good doctor to my right this morning asked me two questions; one was, "Why do we stand erect?" I told him, "I don't know." Some one, however, has answered that question by saying that there is a continuous self-balancing by unconscious move-

\*The almost revolutionary studies of recent years made of plant structures as related to medicinal activity, makes this paper one worthy of being kept before the profession. We therefore take the liberty of reprinting from the *Eclectic Medical Journal*, December, 1920.—Editor.

†Reprinted from the *Eclectic Medical Journal*, November, 1921.

ments of the muscles. The problem has been made a study long ago, but is too far away from pharmacy for me to intrude.

The second question was, "In your laboratory you exhibited to us the Brownian Points, those eternally whirling, never-stop entities that seem to have motions of their own. May I ask, do they whirl in the night? Are they still when it is perfectly dark?" I had never thought of that problem, and I answered, "I don't know."

We do not know when we look through a film of liquid so thin that it separates two parallel glasses, that point, magnified under the ultra-microscope is seen to contain thousands of whirling points as bright as miniature stars. Likened may they be to twinkling star dust of space in the infinitely little. The question, "Do they whirl in the night?" is, so far as I know, unanswered. "Is it light that makes them whirl?" I don't know. I would like to say, in this connection, there is but one Chemist, and Alchemist, the Creator of all things. Let me illustrate. I have some specially made apparatus on this table. Whatever I desire to illustrate necessitates apparatus devised for that specific purpose.

Listen: The Alchemist I mention, by means of a little dirt, a little water and a little sunshine, brings life into a seed, and it becomes something unexplainable. A little dirt, water and sunshine, then comes a living sprout to grow into its own kind—blossom, fruit—and give of its life current vitality to a new crop of seeds that carry the parent stock to generation after generation. Not one life-carrying seed, even microscopic in size, has man, with all his apparatus and presumed scientific knowledge, ever formed.

Listen: Some years ago a talented biologist in Chicago announced that artificial life had been evolved in sea creatures by stimulating their eggs into life, "fertilizing" them by dilute saline liquids. Probably the public press grossly exaggerated his statements, or even perverted them into the assertion that he had *created* life artificially. At that date I chanced to be in New York City and defended the biologist as probably being misquoted, or underquoted, and at the same time challenged the life creation argument. "If he makes the egg, then vitalizes it, I will accept that he has produced life artificially," I said. Has it ever been done? But to return to our subject.

*Concerning Light and Heat.*—Prof. Crooks discovered that if across an exactly balanced rod that rests on the point, be placed four

very light arms, the end of each carrying a small tissue, black on one side and white on the other, when the device is put in the light it begins to revolve. He announced (or at least accepted) that this movement resulted from the action of light striking the white side and being absorbed by the black opposite. After investigating it thoroughly, however, he decided that it was not light, but heat, that made the object move.

Now we know that force-driven materials are nothing marvelous. Electricity moves matter, heat moves matter, magnetism moves matter. There is nothing marvelous about it, unless we attempt to get at the origin of it all, then all is a marvel, a mystery. At a meeting of the American Pharmaceutical Association that met in Niagara Falls thirty-five years ago, Professor Carpenter, the famous English physiologist, was visiting Niagara Falls. We invited him to give a lecture before the Association. He had a friend in England renowned in a different line, in chemistry. His name was Crookes. These two friends, it has been stated (if memory serves correctly), became interested in the phenomena of spiritualism and concluded they would investigate it scientifically. Reading the same books, without bias, as they thought, studying the problem carefully, each with an open mind, Carpenter became a pronounced opponent of the cult, Crookes a devoted spiritualist. Possibly my memory is at fault concerning details, possibly my informant was mistaken in his narrative—it matters little, the text remains and is but a parallel of discordant views, good men hold in all walks of life.

This is what I ask you to accept in the direction of what, as an opinion I bring before you today. I am looking at the problem from one angle. Another year I may look at it differently. How easy it is to differ from one another, and how indiscreet to get out of humor with each other. We do not agree with our own selves after an interval of time.

Two weeks ago I sat in a little circle of men whose names are well known throughout the country. It was an evening dinner. Discussions arose, first one thing and then another. Finally I was called upon to say something. They had been talking on different problems connected with pharmacy and medicine. I said: "Gentlemen, I am here as an invited guest, as you know, a representative of, as I believe, a misunderstood, ostracized section in medicine. I have for a lifetime given my time and study largely to problems that concern the

therapeutic agents developed by members of this section. It may not be improper for me to add that our dominating ideal is that of service of humanity—service to anybody and everybody needing our help—yes, service to those who not only ignore us but too often seek to paralyze our efforts. The historian who studies the records of the past will discover that our aim has been to aid not only our associates, but those who consider it proper to become our enemies. I stand as one who believes himself by age and experience to be competent to balance problems, that in the passing along, where whilst passion prevailed, it was impossible to balance. I have learned to bear no personal animosity against any man who looks at a subject differently than myself. I have resisted what I thought to be wrong, but with no evil intent, for I have never hated any one. Long since have I divorced personalities from issues.”

The next day one of the party met us and said: “Lloyd, do you know what impressed me most of all in your remarks? It was that policy of advocating an issue and forgetting the man—the principle of not making a personal antagonist of the party on the other side.”

Let me now introduce the subject that I came before you to discuss. I have here something to show you, in the light before me today, but I crave the privilege of changing my opinion if future events lead to a reversed view.

For thirty or forty years in the experiments I have made with drugs, plants and plant structures, I have met continuously the fact that linked with each plant texture there was something present that under the influence of an alkali gave a yellow color. For example, strip a pawpaw of its bark and touch the white inner surface with a solution of potash—now it turns yellow. There is probably one rule in this as elsewhere, and that is the rule of exceptions. I hope to find one white blossom that will not turn yellow. If I do, the exception may be of help to the botanist, for it may be the forerunner of a class distinction.

For years this yellow phenomenon was before me, but I could not catch the material that produced it. About a year and a half ago I decided that if I isolated this yellow something that pervaded all plant tissues so linked with impurities as seemingly to defy isolation, it must be obtained from something that is white, something that does not carry a mass of extraneous material to contaminate the principle

desired. Then it occurred, why not use the petals of a *white* flower to get this *yellow* something?

The elder was then in bloom. These, I found, turned deep yellow with ammonia gas. I procured fifty pounds of elder flowers, put them in a percolator, made a tincture, and worked it by means of neutral solvents and excluders, to rid the product of the alcohol, chlorophyl and wax. I had five gallons of the chlorophyl-free liquid, and said to Mr. Miller, who was assisting me: "Place the jar in a cold situation and tomorrow morning I shall examine it." Next morning I tipped the jar very carefully, and all down the sides were little white concretions about the size of pin heads. It was the thing I have been seeking for years.

I took one of those pin heads to the laboratory and dropped it into distilled water and it did not dissolve. I added ammonia—behold! it immediately dissolved, the liquid turning deep yellow. It was only the size of a pin head, but there were thousands of them. And they kept increasing in size. The marvelous phase of this subject is I got eleven ounces (crude) of that substance out of that fifty pounds of elder flowers. Before that, by reason of faulty research, I could not get a grain from anything.

The first thought of a pharmacist is what value a new substance may have in medicine. Alas, the greater part of my work has been the repeated finding of something that had no value. I sent some of this material to Professor R. Adams Dutcher, University of Minnesota, requesting that he make a physiological examination of it. His preliminary report was to the effect that, according to a preliminary investigation, it has no physiological action. May I not ask, should a peculiarity of action be expected of a substance pervading plant tissues everywhere?<sup>1</sup>

In this cylinder I have distilled water, and I propose to put into the water a small amount of this material. Note that it settles to the bottom. It is perfectly insoluble. One grain shaken with a gallon of water apparently disappears, but if let stand until the next day, behold, it is all at the bottom. I now shake the mixture, and pour half of it into another cylinder, then add a little ammonia

<sup>1</sup> I had vitamins in mind. There was reason to hope that a general life supporter of plant life, serviceable to animals, could be found and isolated—not a poison of energetic action. This I accept, Dr. Dutcher demonstrated as a fallacy in the direction of this substance.

water—note the change in color to deep yellow. A very delicate reagent is it for an alkali. Let us now make both liquids yellow. Into one I pour dilute sulphuric acid, in excess, to destroy the ammonia. The liquid becomes colorless.

Now the question came to me, "Why is the white flower white when it has the yellow material in it in such quantity?" Then I figured to myself, it must be because the white petals carry also an acid which in contact with the yellow material makes it white. In other words, would the white flower be yellow if there was an alkali in the petal instead of an acid? Crushing the flower in a mortar with a little distilled water gave a sharp acid reaction. Blue litmus turned red at once. The acid was present.

The question arises, What is the use of this thing in nature? I think I comprehend the subject, but it is too great to try to bring before you today.

I am going to ask you to be charitable in what I have said concerning the theories I now hold. I may be right and I may be wrong. We can see this color change and we know that the petals hold organic acid. What of it? I don't claim that anything I have brought is new; quite the contrary. So far as I know, this experiment has not been made. In some literature unbeknown to me it may be explained. It doesn't matter whether it is new or old—it is a phase in plant economy that is a fact, and may be of service other than as a medicine.

I asked myself, Why could not the material be used to make a test paper? Why would not paper saturated with a solution of this material turn yellow with alkali and colorless with acid? I tried it and it worked. There is a shade between red and blue litmus which makes it difficult sometimes to quite determine the end reaction. There is no intermediate shade with this.

*For example*, let us now pour into these tumblers some water, and into the one put some ammonia and in the other dilute sulphuric acid. The paper I hold in my hand has been saturated with a weak solution of this material and dried. I dip it into the acid. See, it is colorless. Now I dip it into the ammonia; it instantly turns yellow.

You ask the name of this material. I call it *Eldrin*. But it may have been long known elsewhere and recorded under a different name or different terms.



## A ROUTINE TEST FOR THE PRESENCE OF SULPHITES.\*

BY ALBERT E. PARKES.

The following method has been found to be a useful routine one for the detection of sulphites added as a preservative or bleaching agent to foodstuffs, confectionery, and other goods.

It is a modification of the combined methods of Schmidt (*Arbeiten aus dem Kaiserlichen Gesundheitsamte*, 21, 226) and of Winton and Bailey (*J. Amer. Chem. Soc.*, 1907, 29, 1499), and in practice has been found to be speedy, sensitive, and efficient, without the disadvantages of the better-known method of reduction by means of zinc to hydrogen sulphide (*U. S. Dept. Agr. Bul.*, 107, A. O. A. C.).

Ten grms. of the material, such as dried fruit or minced meat or fish, are incorporated with 10 to 20 cc. of water, by means of a pestle and mortar, and transferred to a small conical flask of about 50 cc. capacity. In the case of fruit-pulp, glucose-syrup or fruit juice, 10 cc. may be diluted, when necessary, with 10 to 20 cc. of water in the flask.

Ten cc. of dilute sulphuric acid of about 2N-strength and two or three small fragments of marble chips are now introduced into the flask, and the mouth immediately covered with a piece of starch paper (impregnated with a 1 per cent. starch solution), which should be screwed round the neck of the flask, and held in place with a rubber ring. The reason for the addition of the marble is to set up a gentle current of carbon dioxide to sweep out the oxygen and the liberated sulphur dioxide. The top of the paper is moistened with 1 drop of a 1 per cent. solution of iodine.

In the presence of any appreciable quantity of sulphites the blue stain on the starch paper will be immediately discharged by the sulphur dioxide. If traces only be present, it may take a few minutes. The action takes place in the cold; it may be hastened by leaving the flask in a warm place.

If the drop of iodine solution used be of the magnitude of 0.1 cc. it is obvious that the limit of sensitiveness of the test is the quantity of sulphur dioxide necessary to reduce the iodine and discharge the blue color—namely, 0.00025 gm.; and this is the limit usually found when using known amounts of sulphites, showing that prac-

\*From *The Analyst*, October, 1921.

tically the whole of the liberated gas is driven out of the flask. This amount, if 10 grms. of the material be taken, would represent 0.0025 per cent. of sulphur dioxide, 0.175 grain per lb., or 1.75 grains per gallon respectively.

By using a weaker solution of iodine the test could be made more sensitive, but for a routine qualitative test the strength suggested makes it sufficiently delicate for the amounts usually met with.

Traces of hydrogen sulphide do not seriously interfere with this method, but in practice 1 cc. of a 5 per cent. solution of copper sulphate is added to the other ingredients when testing meat or fish, and this will retain as much hydrogen sulphide as is likely to be present.

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## DECOMPOSITION OF ATROPINE.\*

By D. B. DOTT.

Though it is a well-recognized fact that atropine or hyoscyamine is readily saponified by soda or baryta, forming tropine and tropate, there seems little information available as to the stability of the alkaloid under other conditions. The following experiments are of interest:

1. A weak solution of atropine sulphate was divided into three portions of 20 cc. each: (a) without any addition; (b) with 2 cc. dilute sulphuric acid; (c) with 6 cc. dilute sulphuric acid. After eighteen hours the alkaloid was determined in the usual way, the amount found being in each case exactly the same, 0.164 gm.

2. A weak solution of the atropine salt was divided into three equal volumes: (a) left plain; (b) with 2 cc. solution of ammonia; (c) with 6 cc. solution of ammonia. After eighteen hours the chloroform-soluble alkaloid was estimated:

(a) = 0.236 gm.

(b) = 0.173 gm.

(c) = 0.133 gm.

3. Solution of atropine salt, divided into three equal volumes; (a) left slightly acid; (b) with sodium carbonate in excess; (c)

\*From *The Pharm. Journ. and Pharm.*, October, 1921.

with ammonia in slight excess. After forty-eight hours the alkaloid dissolved with chloroform, etc.:

$$(a) = 0.236 \text{ gm.}$$

$$(b) = 0.161 \text{ gm.}$$

$$(c) = 0.158 \text{ gm.}$$

4. Solution similarly divided: (a) faintly acid; (b) 0.5 gm. sodium carbonate; (c) 0.5 gm. sodium bicarbonate. After sixteen hours, alkaloid was estimated as usual:

$$(a) = 0.158 \text{ gm.}$$

$$(b) = 0.104 \text{ gm.}$$

$$(c) = 0.144 \text{ gm.}$$

5. Extract of belladonna, diluted, acidified and extracted by chloroform, as B. P. directs, in two equal volumes: (a) left acid for sixteen hours; (b) with excess of ammonia, left for some time:

$$(a) = 0.75 \text{ per cent. as atropine.}$$

$$(b) = 0.63 \text{ per cent.}$$

6. Extract of belladonna, watery acid solution divided into three equal volumes: (a) left for sixteen hours, and alkaloid quickly determined in usual way; (b) with excess of sodium bicarbonate; (c) with excess of ammonia, also left for sixteen hours before extracting the alkaloids:

$$(a) = 1.03 \text{ per cent.}$$

$$(b) = 0.91 \text{ per cent.}$$

$$(c) = 0.52 \text{ per cent.}$$

7. Extract of belladonna, aqueous solution similarly divided and treated, the alkaloids being estimated in each case after forty minutes:

$$(a) \text{ left slightly acid} = 1.00 \text{ per cent.}$$

$$(b) \text{ excess of sodium bicarb.} = 0.94 \text{ per cent.}$$

$$(c) \text{ excess of ammonia} = 0.86 \text{ per cent.}$$

The results, no doubt, vary according to concentration of the solution, as well as to proportion of alkali to alkaloid. It might be worth while to try comparative experiments with hyoscyamine and atropine, as to rate of decomposition under the same conditions.

It is evident that the belladonna alkaloids are saponified to a considerable extent when their solutions are left for several hours in contact with ammonia or sodium carbonate, and to an appreciable degree even with sodium bicarbonate. It is true that when only a slight excess of ammonia is added, and the extraction with chloroform is promptly performed, the loss is very little, but the Pharmacopœia is silent on the question of excess, and gives no warning against delay in extracting. When the mixture becomes partially emulsified, and only slowly separates, the operation of extracting with chloroform is apt to be somewhat prolonged. One's attention is sometimes called to a matter which is more pressing, and an assay which has begun is left over for a while. In any case, it is safer to use sodium acid carbonate, and to avoid ammonia and alkaline carbonate when dealing with solutions of atropine or hyoscyamine salts. In the process given for assay of belladonna leaves, in which the drug is percolated with ether-chloroform mixture in presence of excess of ammonia, the result must be appreciably under the truth, as extraction by percolation is not a very rapid process.

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## MEDICAL AND PHARMACEUTICAL NOTES

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CHENOPODIUM OIL.—Dr. Henry and Mr. Humphrey Paget, of the Wellcome Chemical Research Laboratories, contributed a paper to the meeting of the Chemical Society of London on Thursday, October 20, 1921, on this subject, in which it was pointed out that the oil has acquired considerable importance in recent years owing to its use as a remedy for hookworm in the tropics, especially by the International Health Board of the Rockefeller Foundation. The oil has been repeatedly examined since 1908, and it is well established that its principal constituent is ascaridole,  $C_{10}H_{16}O_2$  a liquid peroxide to which the anthelmintic properties of the oil have been generally ascribed until Hall and Hamilton in the United States asserted that the lower boiling fractions of the oil, that is the terpene fractions, were more active in this respect.

The authors have therefore re-examined the oil with a view to isolating its components in a pure state and having them examined

pharmacologically and clinically. This work is being done by Dr. Wilson Smillie, at the Instituto de Hygiene, San Paulo, Brazil, who has already obtained a number of interesting results. The authors find that the oil is essentially a mixture of from 60 to 70 per cent. of ascaridole with hydrocarbons and a small quantity of the decomposition products of ascaridole. The hydrocarbons present are p-cymene, *l*-terpinene and a new terpene, which is probably a dihydro-p-cymene, boiling at 177-178, and yielding a well-crystallized tetra-bromide melting at 117° C. It is probably this tetrabromide, which was mistaken by Nelson for 1-limonene tetrabromide and led to his assumption that the oil contained 1-limonene. The two are, however, quite distinct, the new tetrabromide being optically inactive though derived from a levorotatory terpene and forming monoclinic crystals, whilst 1-limonene tetrabromide is levorotatory and forms rhombic crystals. No evidence of the presence of sylvestrene, safrole, camphor or phelandrene, all of which have been suggested as present in the oil, could be obtained. Minor constituents are butyric acid and methyl salicylate. In the course of oxidizing the hydrocarbon fraction it was found that *l*-terpinene yields two forms of *ld*-dihydroxy-*-methyl-l*-isopropyladipic acid  $\text{CCOH} \cdot \text{C}(\text{Me})\text{OH} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{C}(\text{Pr})\text{OH} \cdot \text{COOH}$  instead of a single form only as stated by Wallach and that both forms are optically inactive.

The clinical results already available show that the constituent of value for the treatment of hookworm is ascaridole and that the hydrocarbon fraction, when pure, has no action on hookworm. The products formed by the decomposition of ascaridole by heat are also quite inactive in this respect.

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TESTS OF PINE PRODUCT DISINFECTANTS.—The disinfectant action, method of production, and chemical properties of pine-oil and pine-distillate product emulsions are reported in United States Department of Agriculture Bulletin No. 989, by the Bureau of Chemistry and the Insecticide and Fungicide Board, as the result of a bacteriological and chemical study of these products.

The work was undertaken for the purpose of determining the physical, chemical and disinfectant properties of pine-oil and other pine-distillation products, in order to secure data to assist in the detection of the adulteration of commercial products as well as to check up the statements concerning the deterioration of pine-oil dis-

infectant and its peculiar behavior against certain pathogenic organisms.

The results reported will be of interest to bacteriologists and chemists who are concerned with testing pine-oil and pine-distillate product emulsions and to hospital authorities, dentists, sanitarians and others who use these products as disinfectants. The investigators found that these products, while effective against *B. typhosus*, are not effective against *M. aureus* and *B. anthracis*, and should not, therefore, be used for general disinfecting purposes. When using pine-oil emulsions against *B. typhosus* it is safer for practical purposes, according to the report, to employ a solution five times the strength capable of killing the organism in five minutes. Thus, a product showing by the Hygienic Laboratory method a killing power of  $\frac{1}{500}$  should be used in a  $\frac{1}{100}$ , or 1 per cent. dilution. If the product will not give a dilution of such a concentration and remain completely emulsified, it should not be used as a disinfectant.

Copies of Bulletin No. 989, giving data upon which conclusions are based, may be had upon application to the Division of Publications, Department of Agriculture, Washington, D. C.

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## SCIENTIFIC AND TECHNICAL ABSTRACTS

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DETERMINATION OF SUGAR IN NORMAL URINE. — Benedict and Osterberg (*Jour. Biol. Chem.*, 1921, 48, 51), describe the following method which in their hands, after extensive trial has given good results. The sample should be diluted so that the sp. gr. is not above 1030. Fifteen cc. are mixed with 1 gram of purified bone charcoal (see below), shaken occasionally during ten minutes, and filtered through a dry filter. Not more than 3 cc. of the filtrate should be used for the determination, and the amount used should contain about 0.001 gram sugar. The volume should be measured into a large test tube which is marked at 25 cc., and if less than 3 cc. of the sample is used water should be added to make up to this volume. One cc. of a 0.6 per cent. of picric acid solution prepared from the dry acid, 0.5 cc. of a 5 per cent. sodium hydroxide solution are added and then 5 drops of a 50 per cent. acetone solu-

tion. This last solution should be not over twenty-four hours old as it does not seem to keep well. The contents of the tube are well mixed and promptly placed in boiling water. The acetone solution should, therefore, be added just before the immersion is made, and all solutions should be added so that no portion falls on the side of the tube. The heating continues for about fifteen minutes. A comparison solution is prepared by heating simultaneously a solution of pure glucose (presumable dextrose is intended), using 3 cc. of such solution containing 0.001 of the sugar. Such a solution will keep indefinitely if mixed with little toluene.

The bone black is prepared by boiling 250 grams of commercial bone black in 1500 cc. of dilute hydrochloric acid (1 to 4 volumes water), for thirty minutes, filtering off hot and washing until the filtrate is not acid. The material is then dried and powdered. The highly absorbant animal charcoals are not suitable. The purified bone black should be tested to prove that it has no sugar absorbing power. The standard and sample must correspond in sugar content within close limits, so that with samples containing very small amount of sugar a more dilute standard will be found more satisfactory.

H. L.

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ANTIDOTES TO COCAINE POISONING.—A child, ten years of age, who had been poisoned with a 10 per cent. solution of cocaine applied to the nose, exhibited strong motor excitation accompanied by pupil dilatation, with very frequent pulse, and numbness. Hoping to counteract the effects of the cocaine, the author injected 0.01 gm. of pilocarpine with the idea of compensating the cocaine effect and also to produce a rapid sweating and diuresis which would be likely to remove the poison rapidly. The result was apparently very rapid; in a few minutes the patient became quieter, and in ten minutes was conscious. A repetition of the procedure upon dogs was not successful. It appeared that the conditions of sweating were not comparable, nor were the symptoms of cocaine poisoning in dogs controlled by amyl nitrite and physiological saline. The trial of sleeping drugs was then resorted to—chloral hydrate, veronal, and scopolamine hydrobromide. Of these, veronal proved to be the best, especially when given intravenously.—A. Hofvendahl (*Biochem. Zeitschr.*, 1921, 117, 55, through *The Pharm. Journ. and Pharm.*, 1921, 287.)

PHARMACOLOGICAL EVALUATION OF CONVALLARIA MAJALIS.—Dr. S. G. Zondek finds that convallaria contains an unusually high per cent. of glucoside, which acts on the heart. The activity, measured on frogs, is five times that of digitalis. The flowers are the most active part of the plant. The M. L. D. of convallamarin per gram of frog was found to be 0.015 mgm. Extracts made with water, 70 per cent. alcohol, and absolute alcohol all showed about the same activity. The relative potency of the herb, flowers and roots is reported as 6000, 10,000 and 5000. The stability of the tincture was investigated with the result that two samples of tincture made from different specimens of the herb and one made from flowers, after standing one year showed only 10 per cent. change, one sample showing an increasing activity. The author concludes that it is possible to standardize tincture of convallaria accurately by the frog method and that the drug is worthy of more extended use.—*Archiv. Exp. Path. u. Pharmacol.* 90, pp. 277-87 (1921).

J. F. C.

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NEW COLOR REACTIONS OF QUININE.—An (aqueous?) solution of a quinine salt is treated in a test tube with chlorine water. To this there is added in such a way that it will form the lower layer, a very dilute ammonia or caustic alkali solution which is saturated with sodium chloride in order to increase its density. At the interface a violet red ring appears while the lower layer is colored green, if ammonia was used, or yellow with potassium or sodium hydroxides. In the erythroquinine reaction, a solution of quinine treated with either chlorine water or bromine water, and then with potassium ferrocyanide, gives a red color. The author, attributing this reaction to the formation of ferricyanide, has modified it as follows: The quinine solution is added to a slight excess of either chlorine water or bromine water, and ammonia is added to slight alkalinity. A green (thalleoquin) color results. If a few drops of freshly prepared solution of potassium ferricyanide are added the green color changes to red, and on shaking the mixture with chloroform, the red color passes into the lower layer.—(D. Ganassini, *Bolletino chim. farm.*, v. 60, p. 141 [1921].)

J. F. C.



THE REACTION OF BALJET; IDENTIFICATION OF DIGITALIS GLUCOSIDES.—The reagent consists of equal parts of 1 per cent. alcoholic picric acid, and 10 per cent. sodium hydroxide free from carbonate. In the presence of glucosides it gives a red or orange color due to isopurpuric acid. The reaction is apparently due to the presence of a lactone group. Wischo concludes that this reaction cannot be used for the quantitative determination of digitalis glucosides because the different glucosides in digitalis galenicals give colors of variable intensity. The strophanthin colors are constant.—(Fr. Wischo., *Zeit. d. allg. oesterr. Apoth. Verein.*, v. 35 [1921].)

J. F. C.

CINCHOPHEN, TOLYSIN AND RENAL EXCRETION.—Phenylcinchoninic acid and the methyl ester of p-methylphenylcinchoninic acid (tolysin) exercise a general stimulating effect on kidney excretion. The action is most marked in the case of uric acid, but it is possible to demonstrate a similar action in the case of urea and chlorides, provided cases are selected with a slightly high blood concentration of these substances.—(Myers and Killian, *J. Pharmacol. Exp. Ther.*, 18, p. 213 [1921].)

J. F. C.

DETECTION OF VERONAL AND VERONAL DERIVATIVES.—Veronal and its derivates may be detected in the urine or intestinal contents when it is present in very small amounts by the following procedure. Two ml. of the urine are shaken out with 2 ml. of ether, the ether is separated and evaporated on a watch glass when veronal, if present, is left in rings which, under the microscope, are seen to consist of needle-shaped crystals. The identification may be checked by adding a few drops of a solution of mercuric oxide in 2.5 parts of nitric acid.—(Zimmermann., *Apoth. Ztg.*, v. 35, p. 382 [1921].)

J. F. C.

ODORLESS PETROLEUM.—This may be prepared by adding 100 gm. of chloride of lime to 4.5 litres of petroleum and shaking. The excess of chlorine may be removed by pouring off the oil onto quicklime, shaking, letting settle and pouring off the clear oil.—(*Pharm. Post*, v. 54, p. 175 [1921].)

J. F. C.

TO DISTINGUISH OUBAIN FROM STROPHANTHIN.—A few crystals of the substance are added to a mixture of 4 to 5 ml. of concentrated hydrochloric acid and a small pinch of resorcin in a test tube and the mixture is heated at 60-70 in a water bath for several minutes. Strophanthin gives a rose coloration; ouabain gives no color.—(A. Richaud, *J. de Pharm. Chém.*, v. 113, p. 161 [1921].)

J. F. C.

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## NEWS ITEMS AND PERSONAL NOTES

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The augmented faculty of the Philadelphia College of Pharmacy gathered together at the festive board, on Monday evening, October the 24th, at Kugler's Restaurant. This initial gathering marks the opening of the series of monthly faculty meetings which have been the custom for some years past. The new members of the faculty were introduced and were given the glad hand of welcome. The monthly meetings of the faculty have been inspirational and educational and are zealously attended by every member of the instructional corps of the College. Scientific papers are usually read by individual members of the faculty, these papers subsequently appearing in the College publication, THE AMERICAN JOURNAL OF PHARMACY.

The course of lectures on popular subjects was opened to a well attended house on October 6, 1921, when Dr. Henry Leffmann, Lecturer on Research at the College, delivered an address on "The Chemistry of Other Worlds." The wisdom of the persons who suggested this course of lectures was reflected in the high-class type of audience that attended this first address. Prof. Freeman P. Stroup, Professor of Chemistry at the College, on October 20, 1921, delivered the second lecture on "Petroleum Products and Their Modern Uses." A working model of oil well machinery, hand-carved by the lecturer, was an interesting exhibit at this lecture which was also listened to by an appreciative audience.

The rehabilitated and renovated College found its annual sessions opened to record breaking classes of students. The elevation of pre-requisite requirements seems not to have materially altered the number of apprentice pharmacists. It was possible, however, to give

comfortable accommodation in laboratory and lecture rooms to all who matriculated.

Fraternities of the College are more active than they have been for many years, and the friendly competition for candidates has been more keen than ever. Their social functions are already under way. The Kappa Psi Fraternity's Smoker on Monday evening, November 7th, proving a success from every viewpoint. The Phi Delta Chi, in their new home at 2021 Green Street, also held a well-attended smoker at the house on Wednesday evening, November 9th.

Professor E. Fullerton Cook presented a paper on the Tenth Decennial Revision of the United States Pharmacopœia before the New York Branch of the American Pharmaceutical Association, evening of November 14th. Other members of the Revision Committee were also present to discuss the revision and its progress.

Dr. Clement B. Lowe, Emeritus Professor of Materia Medica, was presented by the faculty with an engraved gold hunting case watch, a token of their appreciation of his long and honorable connection with the College teaching staff. Professor Lowe, beloved of the students, is no longer teaching at the College, but still maintains an active interest in College affairs and is a regular attendant at the College meetings. The new Professor of Materia Medica, Dr. Horatio Wood, Jr., has already become very popular with his classes.

Dean Charles H. LaWall, along with his multitudinous duties, manages to find time to engage in activities which take him some distance from his usual habitation. For instance, November 10th, at Atlantic City, N. J., he lectured on "Food Adulteration" before their Kiwanis Club. Then at the meeting of the American Public Health Association in New York, we find him reading a paper on "Unsuitable Forms of Cheap Candies" before the Section on Foods and Drugs.

## BOOK REVIEWS

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"COMMON SENSE DRUG STORE ADVERTISING." By Bert Kahnweiler.

There has recently appeared as a contribution to the literature of commercial pharmacy, a 61-page book on the advertising problems of the retail druggist. The author himself is a successful business man and a graduate of pharmacy. He is an enthusiast and justifiably so, since he attributes his own success to the business-getting character of his advertisements.

The book is essentially inspirational, if one may use that term in the commercial world. It at least is stimulating to that sense of business acumen which must be well developed in a commercialized drug store and which is one division of the formula of success. Mr. Kahnweiler has pointed out advertising principles that are practicable and some of the pitfalls to avoid. The book is interesting reading and adds to the growing commercial library of the department-store type of pharmacy.

For sale by the Carey Printing Company. 475 Tenth Street, New York City. Price, \$2.00.

E. F. C.

# INDEX TO VOLUME 93 OF THE AMERICAN JOURNAL OF PHARMACY.

## AUTHORS.

	PAGE		PAGE
Allport, Noel L. An Improved Method of Preserving Specimens for a Herbarium ....	653	Chapin, Robert M. Improved Denigès Test for the Detection and Determination of Methanol in the Presence of Ethyl Alcohol .....	632
Arny, H. V. A Half Century of American Pharmacy .....	639	Clark, R. H. Salicin Content of British Columbian Willows and Poplars .....	618
Pharmacy 100 Years Ago ....	184	Clawson, A. B. The Whorled Milkweed as a Poisonous Plant .....	274
Barker, Lewellys F. The Value of Drugs in Internal Medicine .....	760	Coates, U. Aylmer. Poke Root in Medicine .....	232
Beal, James H. Comment on the Paper of Couch and Giltner on "An Experimental Study of Echinacea Therapy" .....	229	Couch, James F. A Higher Degree in Pharmacy .....	32
Bennett, C. T. Oil of Cade ...	718	An Experimental Study of Echinacea Therapy .....	227
Berghausen, Oscar. Concerning the Therapeutic Action of Some Derivatives of Cod Liver Oil .....	757	Echinacea—A Reply to Dr. Beal .....	324
Beringer, George M. Editorial, I, 2, 73, 155, .....	157	Studies in Extraction. I. The Rate of Extraction of Phyto- lacca Decandra .....	421
The Centenary of Pharmaceu- tical Education in America..	75	The Whorled Milkweed as a Poisonous Plant .....	274
Pharmaceutical Research ....	132	Cunningham, Charles H. Vanilla Production in Mexico .....	272
Bordet, Jules. The Theories of Blood Coagulation .....	701	Davis, Lewis. Studies on Pepsin.	254
Bourquelot, E. Results Attained by the Biochemical Method in the Investigation of Plant Glucosides .....	276	Dohme, A. R. L. The Assay of Aconite .....	426
Braisted, William C. Editorial..	741	Dott, D. B. Decomposition of Atropine .....	863
A Message From the New President of the Philadelphia College of Pharmacy and Science .....	369	Dufilho, E. Preparation and Standardization of the Ex- tract of Nux Vomica .....	266
Cameron, C. R. Brazilian Bati- puta Berries .....	517	Eberle, E. G. Indirect Services of Pharmacy and Pharma- cists .....	125
Carpenter, Wm. H. The Signifi- cance of Education .....	524		

	PAGE		PAGE
Eggleston, W. W. The Whorled Milkweed as a Poisonous Plant .....	274	Hart, William Beamont. The Origin, Development and Value of the Thalleioquin Reaction .....	332
England, Joseph W. High-Lights in the History of the Philadelphia College of Pharmacy .....	604	Hatcher, Robert A. Economy of Time in Percolation .....	534
The Status of Prerequisite Laws and Pharmaceutical Licensure .....	539	Holmes, E. M. Elder Flowers .	557
Evers, Norman. The Titration of Certain Alkaloids .....	656	On the Use of Poke Root in Medicine .....	47
Ewe, George E. The Analytical Characteristics of Powdered Talcum for Use in Toilet Articles .....	316	Horn, David Wilbur. Lactometer and Fat in Milk Control .....	817
Frenkel, M. The Determination of Urea by Xanthidrol ....	264	Houseman, Percy A. Studies on Licorice Root and Licorice Extract. Part III .....	481
Folkstad, C. W. Podophyllum Ash Standards .....	429	Translation: Comparative Researches on the Methods Proposed for the Estimation of Glycyrrhizin in Licorice Root and in Licorice Extract. By Armin Linz .....	376, 455
Foran, Ralph. Smell-Shock ....	683	Hughes, Edward J. Egyptian Secrets and Magical Spirit Art of the Past Ages .....	679
Garvan, Francis P. Address: President of the Chemical Foundation .....	667	Kern, Erwin J. The Determination of Tannin .....	769
Gershenfeld, Louis. Blood Coagulants .....	543	Kirkby, William. Sal Caharticum Amarum .....	551
Gillie, K. B. Salicin Content of British Columbian Willows and Poplars .....	618	Knuth, Richard. Pelargonium Oil .....	302, 376
Giltner, Leigh T. An Experimental Study of Echinacea Therapy .....	227	Kraemer, Henry. Plant Colors .	414
Echinacea—A Reply to Dr. Beal .....	324	Some Experiments on the Modification of Color in Plants	416
Greenish, Henry G. A New Source of Santonin .....	261	Lautenschlager, M. L. Diazo-Reaction of Morphine ....	235
Griffith, Ivor. Editorial 245, 247, 300, 453, 522, 665, 815.		LaWall, Charles H. An Epoch-Making Discovery .....	27
Hackh, Ingo W. D. The Chemical Elements of Living Matter .....	745	Constructive Public Service in Pharmacy .....	546
		Editorial .....	299, 374
		Pharmacy as a Legitimate Science .....	342
		Sour Salt—A New Synonym for Tartaric Acid or Citric Acid .....	496

	PAGE		PAGE
The Founding of the Philadelphia College of Pharmacy and Science .....	167	Newhall, Charles A. The Direct Identification of Soy-Bean Oil .....	147
Visiting Old Friends .....	591	Parkes, Albert E. A Routine Test for Sulphites .....	867
Leffmann, Henry. Editorial ...	589	Paul, Theodor. The Degree of Sweetness of Dulcin and Saccharin .....	260
Recent Advances in Photographic Procedures .....	843	Peck, E. Saville. A Dream of the Future .....	686
The Organo-metallic Bodies ..	621	Peacock, Josiah C. and Bertha L. DeG. Some Notes on the Astringencies of Red Rose and Pale Rose .....	497
Linz, Armin. Comparative Researches on the Methods Proposed for the Estimation of Glycyrrhizin in Licorice Root and in Licorice Extract. Translated by Dr. Percy A. Houseman .....	376, 455	Pearson, Constance E. A New Source of Santonin .....	261
Lloyd, J. T. Spiders Used in Medicine .....	18	Plimmer, R. H. A. The Relative Value of the Proteins in Nutrition .....	645
Lloyd, John Uri. Eldrin, A New Plant Constituent .....	40	Plummer, S. B. Determination of Camphor in Camphorated Oils .....	600
Empirical Fallacies (And Others) .....	627	Polinski, M. Detection of Formic Acid in Acetic Acid ....	236
Plant Constituents .....	861	Prair, David. Professional Training .....	846
McEwen, W. P. Stainless Iodine Ointment .....	277	Price, E. A. An Improved Method of Preserving Specimens for a Herbarium ....	652
Macht, David I. Benzyl Alcohol for Toothache .....	52	Rhodeshamel, H. W. Atropine Sulphate from Datura Stramonium .....	715
Mallanneh, S. A Color Reaction for Aconite .....	444	Roberts, John G. The Volatilization of Ethyl Nitrite from Sweet Spirit of Nitre .....	320
Manseau, M. A. Cocaine and Stovaine, a Different Reaction .....	236	Rogers, C. H. Podophyllum Ash Standards .....	429
Marsh, C. Dwight. The Whorled Milkweed as a Poisonous Plant .....	274	Sadtler, Samuel P. Influence of Pharmacists on the Development and Advance of Modern Chemistry .....	197
Mida, L. M. The Trade-Mark Act of 1920 .....	36	Schöbl, O. Note on the Keeping Qualities of Dried and Pulverized Vaccine Virus ..	143
Merker, Harvey M. Studies on Pepsin .....	254		
Moerk, Frank X. Methyl-Orange as an Indicator in Presence of Indigo-Carmine ....	675		
Newcomb, E. L. Podophyllum Ash Standards .....	429		

	PAGE		PAGE
Sherk, D. L. C. Thymol and Carvacrol Problems .....	8	Wallace, D. A. Determination of Camphor in Camphorated Oils .....	600
Urethanes of Thmyol Carvacrol .....	115, 207	Walton, Lucius L. Some Much-needed Changes in the Practical Experience Requirements of Many Pharmacy Laws .....	839
Sollmann, Torald. The Quinotoxin Myth .....	337	Wellcome Chemical Research Laboratories, The Hyenanchin and Other Constituents of Hyenanche Globosa .....	35
Steinkoenig, Louis A. Concerning the Therapeutic Action of Some Derivatives of Cod Liver Oil .....	757	Wilson, John Arthur. The Determination of Tannin .....	769
Stuart, E. H. Atropine Sulphate from Datura Stramonium ..	715	Winton, A. L. Thomas Franz Hanausek .....	222
Sturmer, J. W. Editorial .....	372	Wood, Horatio, Jr. Schools of Pharmacy as Pre-Medical Schools .....	828
Sycks, Dana C. Cultivation and Distillation of Peppermint in Piedmont .....	348	Youngken, Heber W. Hybridization in Plants .....	249
Tallantyre, S. B. Determination of Bismuth by Formaldehyde .	344	Muir-Puama .....	625
Tuttle, P. V. Notes on Ancient Medicine .....	777	Studies on the Cassaba and Honey Dew Melons .....	104
Van Itallie, L. Peru Balsam and Its Adulteration .....	24		

## SUBJECTS.

A Bounden Duty .....	453	Aconite Assay .....	426
Abstracted and Reprinted Articles ..	515, 551, 627, 686, 760, 846	Color Reaction .....	444
Acetone, Distribution in the Body	56	Aconitine, Resistance to Putrifaction .....	571
Acetosalicysulphate of Quinine .	363	Acriflavine Treatment of Gonorrhea .....	291
Acid, Acetic, Detection of Formic Acid in .....	236	Address of Francis P. Garvan ..	667
Acetyl-Salicylic, Solvent for .	569	A Dream of the Future .....	686
Barbituric, a New Compound of .....	364	Adrenalin, Standardization of ..	515
Benzoic for Detection of Atropine, Cocaine and Stovaine .	287	Adulteration of Peru Balsam ...	24
Formic in Acid Acetic, Detection of .....	236	Alcohol as Locomotive Fuel ....	807
Formic in the Body .....	148	Benzyl, for Toothache .....	52
Hydrocyanic in Linseed Cakes	288	Problem, The .....	589
Iodic, Microchemical Test of .	271	Wood in Grain Alcohol, Test for .....	632
Ipecacuanhic .....	55	Alkaloids, Certain, Titration of .	656
Oxalic, Color Test .....	355	of Valerian .....	731
Picric in Operative Surgery ..	291	Ammonium Sulphate as Weed-Killer .....	727



	PAGE		PAGE
Amylene Hydrate Poisoning,		Biologic Test of Vitamins .....	150
Fatal Case .....	58	Bismuth Determination .....	344
An Inspiration .....	155	Black Draught .....	569
Analysts Laboratory Companion	585	Blood Coagulants .....	543
Ancient Medicine, Notes on .....	777	Coagulation, Theories of .....	701
Antibody Studies .....	450	Body, Distribution of Acetone in	56
What Is An? .....	550	Body, Formic Acid in .....	148
Antibodys, Nature and Origin of	284	Book Reviews 69, 239, 296, 366, 519,	
Antifebrile, New, from India ...	805	584, 663, 811, 878.	
Antiseptics, Research on .....	149	"Books in Running Brooks, Ser-	
Arsenic in Pickles .....	347	mons in Stones and Good in	
Arsphenamine Solution, Toxic		Everything" .....	247
Effects of Shaking .....	360	Botanizing Trip in South Jersey,	
Asclepias Galioides as a Poison-		Account of .....	591
ous Plant .....	274	Braisted, William C., M. D.,	
Assay of Aconite .....	426	Biography of .....	370
Astringencies of Red and Pale		Bricks, Oil of .....	569
Rose .....	497	Buchu, Cultivation of .....	48
Atropine, Cocaine and Stovaine,		Bulletin of the New York Bo-	
Detection with Benzoic Acid	287	tanical Garden .....	663
Decomposition of .....	868	Cade Oil .....	718
Ointment .....	577	Caffeine in Tea and Coffee, New	
from Stramonium .....	570, 715	Method for Determination	
Avian Toxicology .....	146	of .....	560
		and Theobromine, Reaction to	
Baljet's Reaction for Digitalis		Distinguish .....	364
Glucosides .....	875	Camphor in Camphorated Oils,	
Barbituric Acid, A New Com-		Determination of .....	600
pound of .....	364	Carbon Monoxide Poisoning in	
Barium Sulphate .....	815	Closed Garages .....	801
Batiputa Berries, Brazilian .....	517	Carbondioxide Pure, Preparation	
Benzoin, Siam .....	729	of .....	449
Constituents of .....	566	Carvacrol and Thymol Problems	8
Benzyl Alcohol for Toothache ..	52	and Thymol, Toxicity of .....	447
Benzoate in Hypertension ....	60	and Thymol, Urethanes .....	115
Benzoate in Pediatric Prac-		Cassaba and Honey Dew Mel-	
tice .....	291	ons, Studies on .....	104
Esters of the Higher Acids ...	564	Celebration of Founders' Day ..	157
Beta Naphthol in Alcoholic So-		Cells, Reticulated, Staining of ..	154
lution for Itch .....	60	Centenary of Pharmaceutical Ed-	
Bichloride of Mercury Poison-		ucation in America .....	75
ing, Treatment of .....	245	Centennial Address .....	524, 546
Biography of Thomas Franz		Celebration of Philadelphia	
Hanausek .....	222	College of Pharmacy and	
Biological Exploration, Mulford	438	Science, Report of .....	501

	PAGE		PAGE
Charter Members, Original, of Philadelphia College of Pharmacy and Science .....	85	Convallaria Majalis, Pharmacol- ogy of .....	874
Chaulmoogra Oil Derivatives ..	43	Correspondence .....	61
Fractionation of .....	360	Cottons' Process Ether .....	448
Chelerythrine .....	288	Cultivation of Buchu .....	48
Chemical Elements of Living Matter .....	745	of Ergot .....	723
Reactions and Their Equations	519	Cupressus Sempervirens in the Treatment of Hemorrhoids .	448
Chemistry and Analysis of Drugs and Medicines .....	239	Current Literature .....	58, 149
Modern, Influence of Pharma- cists on the Development and Advance of .....	197	Cresol in Lysol, Estimation of ..	733
Organic, A Text Book of ....	813	Denigés Test for Methanol, Im- provement Upon .....	632
Organic, General Industrial ..	296	Dermatitis, Poison Oak .....	568
Organic, Laboratory Experi- ments in .....	70	Determination, New Method of Caffeine in Tea and Coffee .	560
Chenopodium Ambrosioides ....	563	of Tannin .....	769
Oil .....	870	Diazo-Reaction of Morphine ...	235
Chlorine Disinfectants, Germi- cidal Value of .....	286	Dictionary, French-English for Chemists .....	587
Cinchophen, Tolysin and Renal Excretion .....	875	Digitalis, A New Constituent of	563
Clove Oil from Clove Stems ....	356	Glucosides, Identification of ..	875
Coagulants, Blood .....	543	Infusion, Improved .....	357
Coagulation, Theories of Blood .	701	Leaves, Manganese Content of	288
Cocaine and Stovaine, Differen- tial Reaction .....	236	Discovery, An Epoch Making ..	27
Atropine and Stovaine, Detec- tion with Benzoic Acid ....	287	Disinfectants, Germicidal Value of Chlorine .....	286
Poisoning, Antidotes to .....	873	Pine Product, Tests of .....	871
Cod Liver Oil, Derivatives of, Therapeutic Action of ....	757	Distillation of Wood .....	445
Coffee and Tea, Caffeine in ....	560	Draught, Black .....	569
Colchicum Tincture, Identifica- tion of .....	447	Drug Research .....	717
Cold, Effect of on Certain Prep- arations .....	804	Drugs in Internal Medicine, Value of .....	760
Color in Plants .....	414	Dulcin and Saccharin, Degree of Sweetness of .....	260
in Plants, Modification of ....	416	Dyestuffs and Pharmacy .....	299
Commencement Exercises of Philadelphia College of Pharmacy and Science, Re- port of .....	506	Echinacea .....	330
		A Reply to Dr. Beal .....	324
		Therapy, Experimental Study of .....	227
		Therapy, Experimental Study of. Comments on by Dr. J. H. Beal .....	229
		Edestin, Use in Testing Pepsin .	565

	PAGE		PAGE
Editorial 1, 2, 73, 155, 245, 299, 372, 453, 521, 589, 665, 741, 815.		Garvan, Francis P., Address of	667
Education, Pharmaceutical. Cen-		Gelatines and Glues, Determina-	
tenary of in America .....	75	tion of Jellying Power with	
The Significance of .....	524	Polarimeter .....	151
Elder Flowers .....	557	General Chemistry, Introduction	
Eldrin, A New Plant Constitu-		to .....	241
ent .....	40	Genus Eucalyptus—A Critical	
Elements, Chemical of Living		Revision of .....	244
Mater .....	745	Ginger, Tincture of, Treasury	
Elixir Iso-Alcoholic .....	809	Decision on .....	2
Empirical Fallacies (And		Glucose, Haines Modified Test	
Others) .....	627	for .....	794
Emulsion, Sterile Iodoform ....	568	Glucosides, Biochemical Method	
Epsom Salt .....	551	of Investigating .....	276
Ergot, Cultivation of .....	723	Glycerophosphates, Determina-	
Oil .....	729	tion of Small Quantities of	
Ericaceous Plants, Ursone in ..	153	Phosphates in .....	806
Ether, Cottons' Process .....	448	Glycyrrhizin in Licorice Root,	
Ethyl Nitrite, Volatilization of ..	320	Translation .....	388, 455
Eucalyptus for Diabetes .....	59	Green of Plants, Preservation of	289
Examination as a Measure of		Gum Arabic as an Adulterant in	
Ability .....	374	Gum Tragacanth .....	290
Experience Requirement of		Gum Tragacanth, Adulteration	
Pharmacy Laws in Need of		with Gum Arabic .....	290
Change .....	839	Haines Modified Test for Glu-	
Explosives, Dictionary of .....	69	cose .....	794
Extraction, Studies in .....	419	Hanausek, Thomas Franz, Biog-	
Fallacies, Empirical (And		raphy of .....	222
Others) .....	627	Heart, The Power of the .....	791
"Fathers of Old"—Poem .....	182	Herbarium, Preservation of	
Flowers, Elder .....	557	Specimens .....	652
Fluorin Compounds, Poisoning		Heritage, Our .....	73
by .....	153	Histology, Elements of Vege-	
Foods and Vitamins .....	570	table .....	584
Formaldehyde and Paraform-		Honey Dew and Cassaba Melons,	
aldehyde, Determination of,		Studies of .....	104
in Tablets .....	807	Hybridization in Plants .....	24
Formalin in Urine .....	568	Hydrogen Peroxide, Detection of	
Formic Acid in the Body .....	148	Traces of .....	727
Founders' Day Celebration .....	157	Hyenanche Globosa, Its Constitu-	
Founding of the Philadelphia		ents .....	4
College of Pharmacy and		Hyenanchin and Other Consti-	
Science .....	167	tuents of H. Globosa .....	7
		Hypochlorites, Effect of Alkalini-	
		ty on .....	73

	PAGE		PAGE
Idiopathy Toxic .....	362	Luminous Paints .....	730
Indican in Serum as Kidney Function Test .....	60	Lysol, Estimation of Cresol in .	733
Indigo Carmine, Methyl-Orange as Indicator in Presence of .	675	Manganese as a Poison .....	283
Influence of Pharmacists on the Development and Advance of Modern Chemistry .....	197	in Digitalis Leaves .....	288
Infusion of Digitalis, Improved .	357	Magnesium, Qualitative Reaction of .....	449
Insect Powder Dermatitis .....	804	Medical and Pharmaceutical Notes 153, 290, 362, 450, 568, 870	
Inspiration, An .....	155	Medicine, Ancient, Notes on ....	777
Instrument Sterilization .....	290	Meeting, Annual of Philadelphia College of Pharmacy and Science, Report of .....	349
Iodine Ointment, Stainless .....	277	Melons, Cassaba and Honey Dew, Studies of .....	104
Iodoform, Emulsion, Preparation of .....	568	Members, Charter of Philadel- phia College of Pharmacy ..	85
Ipecacuanhic Acid .....	55	Mercuric Chloride Poisoning, Treatment of .....	245
Juniperus Taxifolia, Oil of ....	729	Antidote .....	792
Laboratory Manual for the De- tection of Poisons and Pow- erful Drugs .....	366	Mercury, Organic Compounds of	814
Lactometer and Fat in Milk Con- trol .....	817	Message from the New President of the Philadelphia College of Pharmacy and Science ..	369
Lactose in Milk, Determination of .....	361	Methanol in the Presence of Ethyl Alcohol, Improved Denigés Test for .....	632
Laxatives, Their Mode of Action	789	Method, Biochemical of Gluco- side Investigation .....	276
Laws, Prerequisite, Status of ..	539	New of Quinine Estimation ..	151
Lead Number of Vanilla Ex- tracts .....	806	Methods for Estimation of Gly- cyrrhizin in Licorice Root and Extract. Translation, 388, 455	
Lecithin, Estimation of .....	803	Methyl Bromide Poisoning ....	59
Licensure, Pharmaceutical, Status of .....	539	Methyl-Orange as Indicator in Presence of Indigo Carmine	675
Licorice Root and Extract, Gly- cyrrhizin in .....	388, 455	Metric System, Compulsory Adoption of .....	521
and Extract, Studies on. Part III .....	481	Microanalysis of Powdered Vegetable Drugs .....	298
Linseed Cakes, Acid Hydrocyanic in .....	288	Microbiology, Progress of .....	50
Live Wire Mind, The .....	744	Milk, Alleged Germicidal Prop- erties of .....	281
Cobinal, The Poison of Poison Oak .....	450	Control, Lactometer and Fat in,	817
Cooking Forward .....	372		
tio Calamine .....	573		
lumbi Opio .....	573		
Rubra .....	574		

	PAGE		PAGE
Milkweed, Whorled, as a Poi- sonous Plant .....	274	Oils, Camphorated, Determina- tion of Camphor in .....	600
Mistura Alba .....	574	Essential, Manufacture of ....	345
Ammonize Cum Sengga .....	575	Ointment of Atropine .....	577
Bismuthi Cum Soda .....	576	of Iodine, Stainless .....	277
Rhei Compositus .....	577	of Zinc Ideal .....	728
Rhei Cum Soda .....	576	Oleate of Sodium Action on Gonococcus .....	58
Mitragynine and Mitraversine ..	733	Olive Oil, Test for the Adultera- tion of .....	564
Morphine, Diazo-Reaction of ..	235	One Hundred Years Ago in Pharmacy .....	184
in Viscera, Detection of .....	566	Organo Metallic Bodies .....	621
New Method of Estimating ..	732	Osmotische Untersuchungen ...	811
Muira Puama .....	625	Oubain, Test to Distinguish from Strophanthin .....	876
Mulford Biological Exploration	438	Our Heritage .....	73
Muscarine, An Interesting Alka- loid .....	287	Oxalic Acid Color Test .....	355
News Items and Personal Notes, 237, 292, 365, 451, 518, 583, 663, 734, 809, 876.		Paints, Luminous .....	730
Nutrition, Relative Value of Proteins in .....	645	Peanut Oil, Chinese .....	358
Nux Vomica Extract, Prepara- tion and Standardization of	266	Pelargonium Oil .....	302, 376
Officers and Members of Board of Trustees, Original of Phil- adelphia College of Phar- macy .....	85	Peppermint Herb, Cultivation of in Piedmont .....	348
Oil of Bricks .....	569	Oil, Piedmontese .....	53
of Cade .....	718	Pepsin, Edestin in Determining the Proteolytic Activity of .	565
Chaulmoogra, Derivatives of .	43	Studies on .....	254
Chaulmoogra, Fractionation of	360	Percolation, Economy of Time in .....	534
of Chenopodium .....	870	Peroxide of Hydrogen, Detec- tion of Traces of .....	727
of Clove from Clove Stems ..	356	Peru Balsam and Its Adultera- tion .....	24
Cod Liver, Derivatives of, Therapeutic Action of ....	757	Petroleum, Odorless .....	875
of Ergot .....	729	Pharmaceutical Education in America, Centenary of ....	75
of Juniperus Taxifolia .....	729	Research .....	132
of Peanut, Chinese .....	358	Pharmacist of Renown Passes Away .....	300
of Pelargonium .....	302, 376	Pharmacology of Convallaria Majalis .....	874
Peppermint, Piedmontese ....	53	Synopsis of .....	297
Sandalwood, Australian .....	278	Pharmacopœial Revision Prog- ress .....	61
Soy-Bean, Direct Identification of .....	147		
Volatile of Pimenta Jamai- censis .....	566		
of Wild Pimento Leaves ....	729		

	PAGE		PAGE
Pharmacy, American, Half Cen- tury of .....	639	Podophyllum Ash Standards ...	429
and Dyestuffs .....	299	Poem—"Fathers of Old" .....	182
and Pharmacists, Indirect Ser- vices of .....	125	Poke Root in Medicine .....	47, 232
as a Legitimate Science .....	342	Poison, Manganese as a .....	283
Constructive Public Service in	546	Poisoning, Antidoting Mercuric Chloride .....	792
Higher Degree in .....	32	Bichloride of Mercury, Treat- ment of .....	245
Laws, Much Needed Changes in the Practical Experience of .....	839	by Fluorin Compounds .....	153
100 Years Ago .....	184	Cocaine, Antidotes to .....	873
Schools as Pre-Medical Schools	828	Fatal with Amylene Hydrate .	58
Scientific, Dawn of a New Era in .....	741	with Methyl Bromide .....	59
Year Book of .....	368	Poisonous Properties of Yew ..	152
Phenol and Salicylates, Estima- tion of .....	802	Polarimeter for Determining Jellying Power of Gelatines and Glues .....	151
Philadelphia College of Phar- macy and Science, Founding of .....	167	Pollution of Water .....	661
High-Lights in the History of	604	Portrait—Dr. Wm. C. Braisted (Frontispiece) .....	369
Report of Centennial Celebra- tion .....	501	Dr. Frederick B. Power .....	434
Report of Semi-Annual Meet- ing .....	795	Preparation and Standardization of Nux Vomica Extract ..	266
Phosphates in Glycerophosphates	806	Prerequisite Laws and Pharma- ceutical Licensure, Status of	539
Photographic Procedures, Re- cent Advances in .....	843	Prescriptions, Foreign .....	578
Pickles, Arsenic in .....	347	Presentation of Medal to Dr. Frederick B. Power .....	435
Picric Acid in Operative Sur- gery .....	291	Preserving Specimens for a Her- barium .....	652
Pimenta Jamaicensis, Volatile Oil of .....	566	Priestly in America .....	243
Pimento Leaves, Oil of Wild ..	729	Professional Training .....	846
Pine Products Disinfectants, Test of .....	871	Program of Free Public Lecture Course, 1921-22, Philadelphia College of Pharmacy and Science .....	734
Plant Colors .....	414	Properties, Germicidal of Milk .	281
Colors, Modification of .....	416	Protein in Food as Cause of Headache .....	356
Constituents .....	861	Proteins, Their Relative Value in Nutrition .....	645
Plant Glucosides, Biochemical In- vestigation of .....	276	Quinine Acetosalicysulphate ...	363
Plants, Ericaceous, Ursone in ...	153	New Color Reactions of .....	874
Hybridization in .....	24	New Method of Estimating ..	151
Preserving the Green of .....	289	Quinotoxin Myth .....	337

	PAGE		PAGE
Report of the 100th Annual Meeting of Philadelphia College of Pharmacy and Science .....	349	Standards of Podophyllum Ash ..	429
Research, Drug .....	717	Sterilization of Instruments ...	290
on Antiseptics .....	149	Stovaine and Cocaine, Differential Reaction .....	236
Pharmaceutical .....	132	Atropine and Cocaine, Detection with Benzoic Acid .....	287
Reticulated Cells, Staining of ...	154	Stramonium, Atropine from 570, 715	
Rhus Dermatitis .....	346	Strophanthin, Test to Distinguish from Oubain .....	876
Root, Poke in Medicine .....	47, 232	Studies in Extraction .....	419
Rose, Red and Pale, Astringencies of .....	497	on Licorice Root and Licorice Extract. Part III .....	481
Saccharin and Dulcin, Degree of Sweetness .....	260	on Pepsin .....	254
Reaction .....	731	Sugar in Normal Urine, Determination of .....	872
Sal Catharticum Amarum .....	551	Sulphites, A Routine Test for ..	867
Salicin Content of British Columbian Willows and Poplars ..	618	Sumac, Italian, Production of ..	282
Salicylates and Phenol, Estimation of .....	802	Sweetening Agents, Definitions and Units of .....	805
Salt, Epsom .....	551	Synthetic Chemical Industry, American .....	665
Sour .....	496	Talcum, Analytical Characteristics of .....	316
Sandalwood Oil, Australian ....	278	Tannin, Determination .....	769
Santonin, A New Source of ...	261	Tea and Coffee, Caffeine in ...	560
in Wormseed .....	808	Test, Microchemical of Iodic Acid .....	271
Schools, Pre-Medical, Pharmacy Schools as .....	828	for Sulphites .....	867
Scientific and Technical Abstracts 149, 284, 355, 447, 563, 727, 801, 872.		Thalleioquin Reaction .....	332
Secrets, Egyptian and Magical Spirit Art of the Past Ages	679	The Dawn of a New Era, in Scientific Pharmacy .....	741
Services, Indirect of Pharmacy and Pharmacists .....	125	Theobromine and Caffeine, Reaction to Distinguish .....	364
Shepherd's Purse, Active Constituents of .....	503	Therapy, Echinacea, Experimental Study of .....	227
Siam Benzoin .....	729	Thymol and Carvacrol Problems ..	8
Constituents of .....	566	Urethanes .....	115
Smell-Shock .....	683	Titration of Certain Alkaloids ..	656
Sour Salt .....	496	Toothache, Benzyl Alcohol for ..	52
Soy-Bean Oil, Direct Identification of .....	147	Toxic Idiopathy .....	362
Spiders Used in Medicine .....	18	Toxicity of Thymol and Carvacrol .....	447
Staining Reticulated Cells .....	154	Toxicology, Avian .....	146
		Trade-Mark Act of 1920 .....	36

	PAGE		PAGE
Travaux du Laboratoire de Matière Médicale de La Faculté de Pharmacie de Paris . . . .	587	Veronal and Derivatives, Detection of . . . . .	875
Travaux du Laboratoire de Matière Médicale de L'École Supérieure de Pharmacie de Paris . . . . .	71	Viscera, Morphine in . . . . .	566
Treasury Decision on Tincture of Ginger . . . . .	2	Visiting Old Friends . . . . .	591
Tripanocidal Action of Arsenic and Antimony Compounds .	359	Vitamin, Fat Soluble and Yellow Pigmentation in Animal Fats . . . . .	803
Urea, Determination of, by Xanthidrol . . . . .	264	Vitamins, Biologic Test of . . . .	150
Urethanes of Thymol and Carvacrol . . . . .	115, 207	in Cooked Carrots and Navy Beans . . . . .	150
Urine, Formalin in . . . . .	568	Distribution of . . . . .	721
Normal, Determination of Sugar in . . . . .	872	and Foods . . . . .	570
Ursone in Ericaceous Plants . .	153	Reserves in the Organism . . .	290
Vaccine Virus, Dry and Pulverized, Keeping Qualities of . .	143	Volatilization of Ethyl Nitrite .	320
Vaccines, Utility of Anti-Plague	359	Wassermann Reaction Outside of Syphilis . . . . .	292
Valerian Alkaloids . . . . .	731	Water Pollution . . . . .	661
Value of Drugs in Internal Medicine . . . . .	760	Weed-Killer, Ammonium Sulphate as . . . . .	727
Vanilla Extracts, Lead Number of . . . . .	806	Welcome 1921 . . . . .	I
Production in Mexico . . . . .	272	Wire Worms, Chemical Constitution and Toxicity to . . . .	285
		Wood Distillation . . . . .	445
		Xyanthidrol Determination of Urea . . . . .	264
		Yew, Poisonous Properties of . .	152
		Zinc Ointment, Ideal . . . . .	728



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